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THE AMERICAN
JOURNAL OF PHARMACY

DECEMBER, 1920

EDITORIAL.

WANTED—BOOSTERS FOR PHARMACY.

The columns of the current issues of some of the pharmaceutical journals again confirm the comment made by a non-interested observer that "much of the pharmaceutical literature of the day has a pessimistic tendency that is far from beneficial to the progress of pharmacy." In the past, we have expressed our opinion of the evil of disparagement[1] and the injury that pharmacy was sustaining from the continuous and deliberate "knocks" in print and public utterances and the disparagements appearing in "pharmaceutical journals." It is with chagrin and regret that we note another of these periodical storms of disparagement and observe that the showers are descending upon the American Pharmaceutical Association, our esteemed contemporary, *The Journal of the A. Ph. A.*, and the management thereof.

We take no exception whatever to any proper comment, objection, or even censure. On the contrary, we believe that constructive criticism is beneficial and on various occasions have exercised this right. There is, however, a wide disparity between fair and just criticism aimed to effect progress or a well thought out improvement and a distorted view that permits of such strange accusations as: "the policy under which the *Journal of the American Pharmaceutical Association* has been conducted for eight years is contrary to the wishes of 95 per cent. of the Association;" "that the prime object of the *Journal* as set forth in the initial declaration of the first editor was for the purpose of restricting its circulation, so that it shall circulate only among its active members;" "that it is worthless as an advertising medium;" "that there was a method in madness by which, in choosing the Committee on Publication, the

[1] Editorial—*A. J. P.*, April, 1919, p. 191.

editors of rival journals were preferred;" that a coterie has been in control of the journal and that these barnacles having about wrecked the ship are now yelling lustily for help."

This tissue of overdrawn, harsh and uncalled for accusations, it would seem had been penned during an attack of dyspepsia or a period of aberration that blotted from memory and barred from sight a more pleasing, characteristic and truthful picture. So absurd are these and other statements contained that refutation would appear as unnecessary. They must fall because of their lack of foundation, their inherent weakness and unbalanced construction. Unfortunately, despite the crumbling into the dust from which such mud pies are made, this derogation of the American Pharmaceutical Association and the aspersion of the motives of those who have so unstintingly devoted their best efforts to its upbuilding, remains as a vicious example of the disparagements emanating from some whose actions are not in harmony with their professed interest in the progress of pharmacy.

It is the duty of pharmacists to uphold the American Pharmaceutical Association and to sell membership therein to every druggist in America. Would any salesman commit such a suicidal act as to advertise to his prospective customers every possible defect or imaginary fault that either had occurred or that might arise in his merchandise.

All products of the human conception are prone to fall short of their ideals and this is but an evidence of the imperfection of man and the limits to his powers and knowledge wisely ordained by the Omnipotent and Omniscient Creator. The American Pharmaceutical Association is but the reflection of the imperfect endeavors of imperfect human beings to effect an ethical development of the commercial and professional aspects of pharmacy. Perfection cannot be expected and the faults of judgment and the errors of management are only the common experiences of all such organizations. In the past, we have frankly criticized some of these defects, however, without at any time questioning the sincerity or motives of its officers. We hold this as the common right of all members. The advocacy of any meritorious action does not require the disparagement of the great work of the Association and the honest endeavors of its active members. True reforms and actual progress are achieved through the orderly processes of evolution working along the paths of established forms and tried legal methods of procedure.

We have watched, with pride, the development of the American Pharmaceutical Association and have been pleased to note the continued extension of its activities in behalf of pharmacy. We firmly believe that these activities can be and will be further expanded as necessities or opportunities present themselves. We even venture the assertion that the further broadening out of its field of usefulness will be accomplished as a result of the sane deliberation of its conservative members and not through the propaganda of "knockers." The upbuilding will be continued on the bed rock of solid facts and accomplishments and not upon the illusionary shadows and day dreams of pessimists. "An ounce of up and doing is worth a pound of being done."

After all, the true measure of success is the service rendered, and this is directly in proportion to the adherence to the purposes of the organization. We wonder if these critics are acquainted with the history of the American Pharmaceutical Association and the spirit that has actuated the leaders thereof from its inception. The space available and likewise the purpose of this editorial will not permit us to present at this time the retrospect that we believe is necessary. However, we urge that the pharmacists give due consideration to the declared aims of the Association, its policies, its continual service in behalf of the advancement of both the scientific and the commercial sides of pharmacy, its research work, its attainments and its scientific publications.

Let each also give thought to what has been the influence of this Association upon his own career; the inspiration and the value of the example of the fathers of pharmacy who through its agency have added so much to the development of our vocation. Have we not cause for pride in their labors which now become our inheritance, and what a wonderful inheritance is ours. In turn, the present generation has the moral responsibility of upholding their ideals and traditions, of maintaining the faith, of continuing the upbuilding of the profession upon the sound principles that have been transmitted to us. Can one picture what would be the condition of pharmacy in America if the American Pharmaceutical Association had not been organized and ever since had not maintained its efforts for the advancement and protection of our calling?

The interests of pharmacy demand that the great body of American pharmacists should be brought into the membership of the A. Ph. A. and educated up to its standards and ideals and not that

these standards and ideals should be debased. Pharmacists must themselves establish and maintain the ethical status of their profession. This cannot be brought about by continuing to sow the apples of discord or the brambles of disparagement.

Equally unfortunate and disastrous to the profession is the attitude of those who favor extolling the position of other professions and decrying the status of pharmacy. The homely philosophy of Rastus' advice are words of wisdom for such:

> "De sunflower ain't de daisy, and de melon ain't de rose;
> Why is dey all so crazy to be sumfin else dat grows?
> Jess stick to the place you're planted, and do the bes' you knows;
> Be de sunflower or de daisy, de melon or de rose."

Pharmacy has no mean inheritance, possesses a history worth extolling and many eminent devotees whose examples are worthy of emulation. The use of the hammer after all requires no great amount of intelligence, just physical strength. Is the "knocker" exercising even his strength to the best advantage? If pharmacy is to come into its own it must be by the very opposite method. The need of the time is for its boosting. Not by a few, but by all of those who claim to be within its ranks. G. M. B.

ISOTOPY.*

By Henry Leffmann A.M., M.D.,

Special Lecturer on Research, Philadelphia College of Pharmacy and Science.

The theory that matter is discontinuous and made up of minute particles which are incapable of diminution in mass or alteration in character, is of great antiquity. In fact, the word "atom" by which these particles are collectively designated, was coined by Greek philosophers many centuries ago, and the general principle stated that the properties of all substances depend on the nature of the atoms, the manner in which they are arranged and the motions they mutually impart and receive, phrases that sound much like those in

*Abstract of an address delivered at a meeting of the Instructional Corps of the Philadelphia College of Pharmacy and Science.[1]

[1] The data for this communication are taken principally from a paper by Dr. Theodore W. Richards (*Science* [n. s.], 49: 1, 1919) and "Introduction a la Chimie Générale," by M. Copaux, a translation of which, by the author of this abstract is about to be published by P. Blakiston's Son & Co.

which modern chemists define their views of combination. The ancient Greeks must have reached their opinion by reasoning alone, for we have no indication that they carried out any experiments, and as they were substantially unfamiliar with the exact physical and chemical properties of gases, it does not seem possible that they could have applied inductive methods.

The atomic theory remained for many centuries unfruitful and merely a philosophic postulate. That it did not lead in Greece to a development of more definite data is probably, in part due to the idealism that overwhelmed the materialism of the early thinkers, but at any rate for many centuries the theory is not active in determining the course of investigation or thought.

In the early part of the nineteenth century, John Dalton propounded the theory in a definite form, and gave to the atom a quantitative relation that made it almost immediately a fundamental datum of chemistry and physics, a position which it has held without material modification until recent years. Dalton's claim to priority in the formulation of the modern atomic theory has been lately challenged by A. N. Meldrum, a Fellow of Bombay University, who, in a paper on "The Development of the Atomic Theory," asserts that William Higgins published substantially the same views about fourteen years before Dalton. This is not the place to discuss the question, but it is to be noted that the modern theory differs from the ancient one in the distinct quantitative relations that the several atoms bear to each other. In the same way the modern system of symbols differs from the earlier ones. The Greek alchemists of the early Christian centuries, had symbols for all the elements they knew, and methods of expressing certain classes of compounds, especially alloys, by associating the symbols, but Berzelius devised the system in which each symbol is not simply an abbreviation of the name of the element or derived from fanciful associations of it, but represents a definite weight in relation to a standard. A combination of the alchemistic signs for mercury and copper represents any proportion of those substances, but CuAg represents a definite proportion by weight.

The theory of the indivisibility and practical inalterability of the atom dominated the physical sciences for nearly a century, but is now materially modified, this modification having been brought about principally by the study of the phenomena of radio-activity. Space does not permit of description of the details of the methods of

research nor an extensive discussion of the present day views, but the following summary will suffice for an introduction to the special subject of this address.

The Electron.—All atoms contain a common constituent, the electron, the discovery of which resulted especially from studies made with the Crookes tube. Differing completely from light, the cathode rays are made up of distinct corpuscles of extremely minute mass—about 1/1700 that of the atom of hydrogen—which corpuscles are negatively charged, and have a high velocity, approximating 50,000 kilometers per second. The velocity is dependent on the electric potential influencing them, but the charge and mass are always the same whatever may be the circumstances of their liberation. The electron, therefore, is a universal constituent of matter.

The Positive Nucleus.—To compensate for the negative charges of the electron, the neutral atom should contain a positively charged mass, which Rutherford considers as reduced to a very small central nucleus, about 0.0001 of the diameter of the whole atom. Around this positive nucleus, in which is concentrated the individuality of the atom and almost its whole mass, the electrons circulate in number about equal to half the atomic weight. Helium (at. wt. 4) has two electrons; carbon (at. wt. 12) has six, and so on, but hydrogen does not follow the rule as it has one electron and a positive nucleus. Moreover, though all electrons are identical among themselves, they probably do not have exactly the same value as constituent particles, for it seems illogical to suppose the same origin for the electrons that are emitted in such peculiar transformations as those of the radioactive substances (beta-rays), as the electrons that are concerned in the simple change of valency when ferrous salts are converted into ferric. In the former instance, the electrons probably come from a deeper and more essential part of the atom than do those in the latter.

It can also be assumed that the electrons are arranged in several concentric groups and be in close contact with the positive nucleus.

One of the results of this structure of the atom is the possibility of transformation of one type of atom into another, in other words, the creation of one element from another. This has been, as is well known, the dream of ages. It has now been shown to be possible, not along the lines in which the search has been made, namely, the conversion of the baser metals into gold, but in the conversion, for instance, of uranium into helium. It has been found that uranium

undergoes spontaneously slow conversion into radium, and that this conversion is accompanied by a liberation of three atoms of helium for every atom of radium produced. Radium further undergoes change by loss of one atom of helium, into a gas termed *niton* or *radium emanation*, and this emanation by loss of four atoms of helium, passes into a form of lead, which differs from lead extracted from the common ores by having a distinctly lower atomic weight. The sequence of change may be represented thus

U	—	He_3	⟶	Ra
238.5		$12(3 \times 4)$		226.5
Ra	—	He	⟶	Nt (radium emanation)
226.5		4		222.5
Nt	—	He_4	⟶	Pb
222.5		$16(4 \times 4)$		206.5

Numerous, carefully made determinations of the atomic weight of lead from the ordinary ores (which are not radioactive) gave 207.2 as the average, but when the same determinations are made on lead from radioactive minerals, which always contain some lead, the atomic weight is, as shown above, sensibly lower.

An explanation that has been offered to account for phenomena of this type is that many of the common elements, if not all, are really made up of two or more closely accordant elements, agreeing in all or nearly all their chemical and physical properties, except slight differences in the atomic weights, and that the differing proportions in which such mixtures occur determine the slight variation in the atomic weights of the elements obtained from different sources. One difficulty in this view is to explain why in certain occurrences of the elements the proportions are always the same, since from such sources, the atomic weights are constant. It must be remembered, however, that the most striking instance of variability, that just set forth, relates to an element occurring under two distinctly different conditions, respectively with and without radioactive association. It must be borne in mind, by the way, that the lead obtained from radioactive ores is not itself radioactive. The emissive power ceases with the production of that element.

In consequence of these capacities of certain elements to change in atomic weight, several of them may be found in the same position in the periodic system, and for this reason they have been called "isotopes," from Greek words "equal" and "place."

An interesting feature of the phenomenon is that there is now exhibited in chemistry a disposition to return to the "whole number" theory of atomic weights. In 1815, Prout advanced the view that all elements are aggregations of the hydrogen atom, which is the lightest known, and hence all atomic weights should be whole numbers if referred to hydrogen as unity. This attractive supposition was soon rendered unacceptable by the researches of Dumas, Marignac and Stas, who showed that the most exact determinations of many atomic weights did not allow of the supposition of their being whole numbers. If, however, the duplex or multiple composition of the common forms of the elements is assumed, it may be, as noted above, that a mixture of two isotopes in certain proportions, though each has a whole number atomic ratio, will give a fractional ratio as compared with hydrogen. Thus, one of the most striking of fractional atomic weights is that of chlorine, the figure for which stands practically midway between two integers. Now if this element is a mixture of two isotopes, having respectively the atomic weights of 35 and 36, it is easy to see that in a certain proportion the mixture will yield a fractional ratio.

Isotopes are so far not separable by chemical means. In this respect, they constitute one step further in analogy to elements long known and separable. The known elements, although only a few score in number, present us with an epitome of the evolutionary relations of nature at large, just as the modern theory of atomic structure presents us with an epitome of the solar system, the nucleus with its more or less loosely held circulating electrons, resembling the sun with planets, moons, meteors, comets and cosmic dust tributary to it. Such elements as chlorine and potassium stand at the extremes of the series, their separation being almost automatic, then the members of the chlorine and potassium groups, respectively, agree closely among themselves, and their separation requires special care. Closer affiliations are noted between, for instance, nickel and cobalt, and still closer between the cerium metals, and, finally, the most recent specific separation of a supposed element into its constituents by chemical means is the decomposition of didymium into two distinct contrasting metals, neodymium and praseodymium, the former producing a series of bright red salts and the latter a series of brilliant green ones. The next problem of separation is that of the isotopes.

THE THEORY OF PERCOLATION.

By James F. Couch,
Washington, D. C.

(*Continued from November number, page 796.*)

THE PERCOLATE.

The immediate product of percolation is the solution which issues from the percolator, the *percolate*. It represents a summation of the various complexes of the precolate and, to a certain extent, furnishes an index to the conditions within the apparatus. The changes which it undergoes are regular and have been the object of much careful study. There are, however, many questions involved which cannot, at present be answered and the whole subject needs revision and extension particularly since much of the study of percolates was made before the pharmacopoeial standard for fluidextracts was changed from a grain per minim to a gram per mil.

The first question which confronts us in this consideration is, what does the percolate represent? With our present knowledge this is exceedingly difficult, if not impossible, to answer. For such drugs as peppermint, ginger, or aspidium, which we percolate with a simple menstruum as alcohol or acetone, thereby dissolving but few of the constituents of the plant while the larger number of them is excluded, the lack of complexity of the precolate enables us to decide that the percolate represents that portion of the drug which is soluble in the given menstruum and the quantitative composition of the percolate bears a direct and simple relation to the degree of exhaustion and composition of the partially exhausted drug then in the percolator.

When, however, we are dealing with drugs of more complex composition, and are extracting them with a complex solvent such as diluted alcohol, the strength of which, and consequently its solvent powers, is variable the answer to the question is not so easy to formulate. As I have fully outlined above, the composition of the precolate is variable under such circumstances, the qualitative composition of the drug varies in different parts of the percolator through physical reactions and, as a result the percolate represents a summation of the conditions within the percolator some of which are mathematically negative and none of which have been satisfactorily investigated. A percolate collected in such a case will vary in the composition of its different parts and this variation will be not only quantitative but qualitative and may lead to precipitation on mixing.[1]

[1] Cf. Lloyd, *Proc. A. Ph.* 1881, 408.

The composition of the percolate depends upon several factors; the nature of the drug, the condition of the drug, the nature of the menstruum, the shape of the percolator, the manner in which the drug is packed in the percolator, and the rate at which the percolate is allowed to flow from the apparatus.

The first five factors have already been considered; the last may profitably engage our attention now. All pharmacists who have devoted time to the study of percolation have recommended that the flow of percolate be retarded to a very slow dripping. Squibb[1] says: "It is an axiom in percolation that the slower it is performed the more perfect and sudden is the exhaustion, and with the smallest quantity of menstruum." Again, for percolating one pound of drug he directs a rate of flow of one drop every two seconds or "about 3 fl. oz. per hour; and for larger quantities in the same ratio."[2] Bedford[3] agrees with this but adds that the rate of flow may be increased toward the end of the percolation. This latter idea as I shall presently show, is erroneous. Lloyd[4] and Procter[5] have also declared in favor of slow percolation.

How slow should we percolate? Obviously the criterion is the strength of the solution which issues from the apparatus; we should control the rate of flow just as we control the time of maceration, that is, in such a way as to obtain as concentrated a percolate as is desirable, not necessarily as concentrated as possible. For we may, by disregarding the time consumed, keep increasing the strength of our percolate at the expense of time, though at a diminishing rate, apparently for months. Time, however, cannot be neglected for it is one of the most important factors pharmaceutically and financially. The time, therefore, which we can allow for the obtaining of a certain amount of percolate is limited and must be gauged, like the time given to maceration, by the operator's experience and judgment.

Squibb allows a faster rate of flow, "in the same proportion," for large quantities of drug. This is open to some further consideration for, as I have already pointed out, it is not practicable to use as fine a powder of certain drugs in large quantities, enough

[1] This Journal, Vol. 39, 400, (1867).
[2] This Journal, Vol. 30, 97, (1858).
[3] *Pharm. Record*, 6, 19, (1886).
[4] *Proc. A. Ph. A.* 1879, 682.
[5] *Pharm. Jour.* 19, 139, (1859).

to prepare ten or twenty-five gallons of fluidextract for instance, as one may use in the much smaller pharmacopoeial amounts, and it is my opinion that, the coarser the drug, the slower should be the rate of flow of percolate.

The time factor will materially influence the rate at which the percolate changes from a nearly saturated solution to nearly pure menstruum so that no mathematical rule which does not take it into consideration can be applied to the variation in the composition of the percolate. We may, however, state in general terms the character of this variation and present a definite idea of the phenomena involved.

Specific Gravity.—The first portions of percolate are laden with extracted matter and are specifically heavier than any succeeding fraction. They may, indeed, present a greater specific gravity than the fluidextract made from the drug due to the fact that they may contain not only more extract but a larger proportion of water which originates in the natural moisture of the drug. If the fractions of percolate are taken in small volumes it may be found that the second fraction is of greater specific gravity than the first due to an actually greater content of extract.[1] As above suggested this anomalous condition is probably due to the first portion of percolate lying during the larger part of the maceration quite out of contact with the drug.

The lowest specific gravity possible is, of course, that of the menstruum and this is the limit which the changing values for the fractions approach. It has been found[2] that the character of the change in the specific gravity of successive fractions as percolation proceeds is quite regular and furnishes a rough indication of the degree to which the drug has been exhausted.

Accompanying the change in specific gravity we find a decrease in the amount of extract contained in the individual fractions, each being a little less concentrated than its immediate predecessor. If the percolation has not been interrupted so that no period of maceration has occurred since the start of flow of percolate, the decrease of extract concentration proceeds with regularity as the following table, taken from one of Lloyd's publications,[1] shows.

[1] Lloyd, This Journal, Vol. 50, 434, (1878).
[2] Squibb, This Journal, Vol. 50, 229, 223, (1878).

TABLE I.

Percolation of 7680 Grains of Cimicifuga.

Fluidounce of Percolate.	Gms. of Dry Extract.	Fluidounce of Percolate.	Gms. of Dry Extract.
1	3.33	13	0.77
2	2.80	14	0.68
3	2.38	15	0.58
4	2.19	16	0.35
5	1.94	17	0.36
6	1.71	18	0.32
7	1.43	19	0.23
8	1.34	20	0.22
9	1.12	21	0.22
10	0.84	22	0.21
11	0.79	23	0.22
12	0.73	24	0.21

These results have been plotted as Chart B and show in a striking manner the uniformity of the decreasing extract content in the percolate. Many similar results from the work of Squibb, Diehl, Robbins and others confirm the fact of regularity in extraction.

When, however, we subject the experimental results to mathematical treatment we discover no expression which applies to the conditions of every fraction. Instead, in the case of every formula which one would expect to generalize the phenomena, we find variation where we should obtain constancy, and, furthermore, the variation appears to proceed in a regular fashion from one fraction of the percolate to the next equal fraction, either increasing or decreasing the "constant," which indicates that a constantly varying factor or set of factors is missing from our data.

What these missing factors are can only be indicated here. I hope to consider this phase of the subject more in detail at some future time when I may present new data. The first factor which may vary is the chemical composition of the extract contained in each fraction. From the evidence presented under the discussion of the composition of the precolate we should expect the first fractions of the percolate to differ qualitatively from those fractions obtained toward the end of the process. This question was investigated by Squibb on cinchona[1] and on podophyllum.[2] He states: "The extract or soluble matter yielded to the menstruum is not

[1] This Journal, Vol. 39, 402, (1867).

[2] This Journal, Vol. 40, 1, (1868).

uniform in its chemical and therapeutical value as obtained during the different stages of the percolation, but diminishes in effective value far more rapidly than the extract does in weight." In support of this statement he reports experimental results showing the

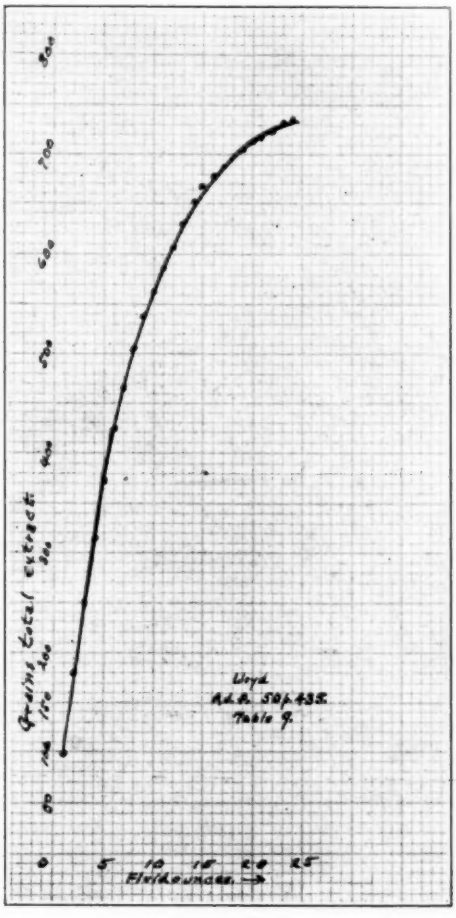


Chart B.

weight of total extract obtained from fraction of a percolate and its content of some active material. These results show conclusively that there is a great difference in the rate at which the various soluble matters of a drug are extracted by the menstruum, and, in the cases which Squibb chose, the pharmacologically important substances

were extracted more rapidly than the inert compounds so that the first portions of the percolate contained a larger percentage of the alkaloids or resin than the total extract. Squibb's[1] results are plotted as Charts C and D and plainly show the phenomenon. Lloyd

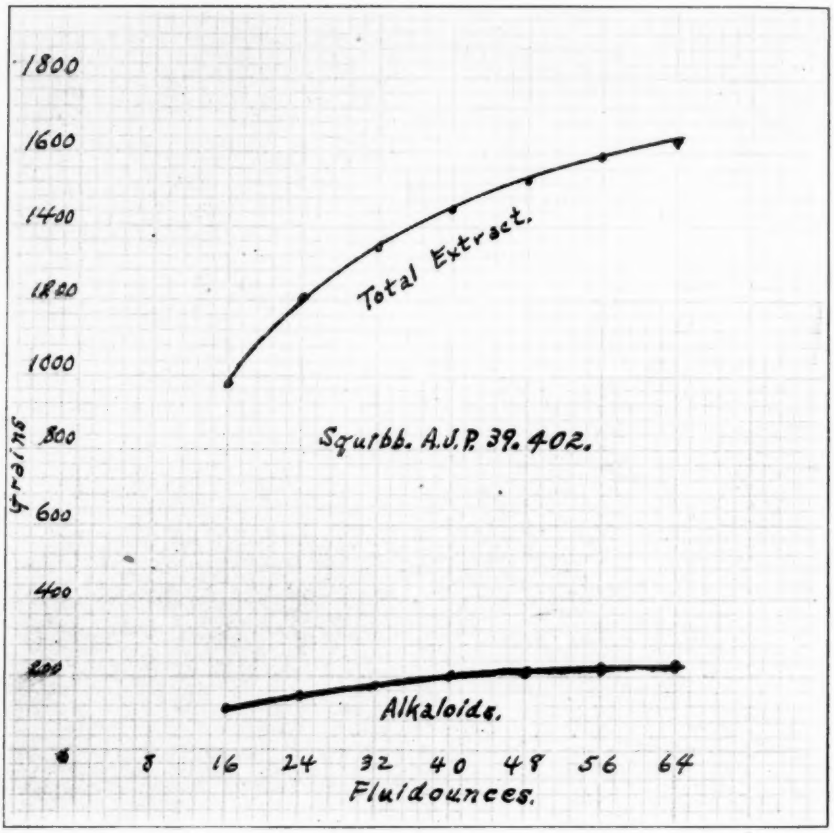


Chart C.

has confirmed this observation by several experiments, notably upon cannabis and cascara.[2]

A second variable factor may arise if menstrua of certain types are employed. These types of menstrua include hydro-alcoholic, glycerinated, and acidulated menstrua. It frequently happens that

[1] This Journal, Vol. 38, 109, (1866.) Vol. 39, 289, 402, (1867).

[2] *Proc. A. Ph. A.* 1881, 408.

the relative proportion of the mixed solvents is not the same in the liquid portion of the percolate as it is in the menstruum and for the following reasons: where acids or glycerin are added to the menstruum the addition is frequently made wholly to the first portions used to moisten the drug so that the bulk of the component is found in the primary fractions of the percolate. With hydro-alcoholic menstrua, which do not usually vary to any great extent throughout the process, other conditions arise which may alter the proportions of alcohol and water found in the percolate.

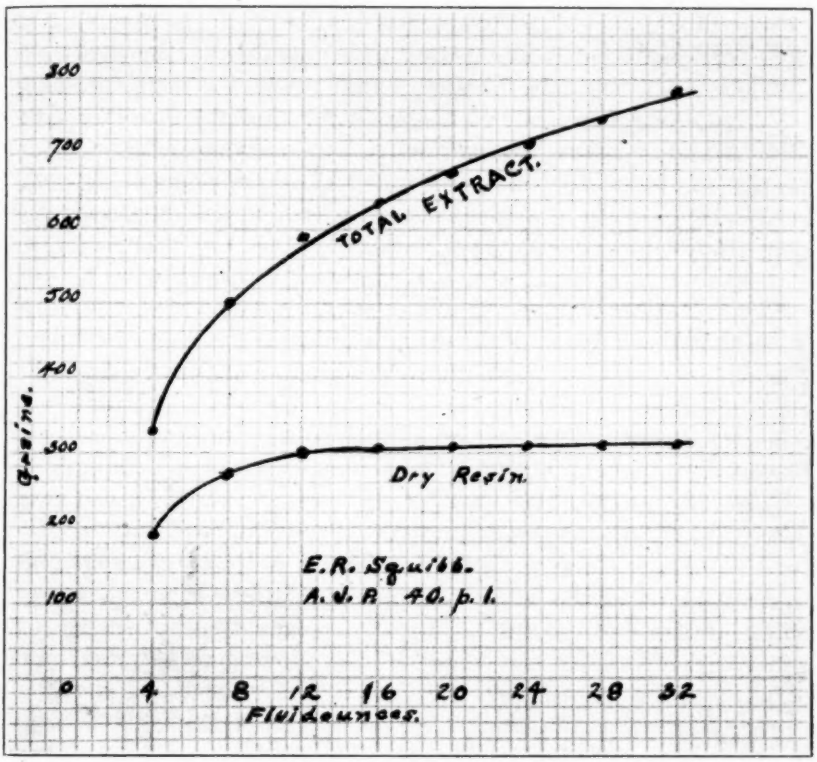


Chart D.

In the first place given a menstruum of high alcoholic content, the first portions of the percolate will contain most of the water which the drug originally held as moisture. This usually averages from six to ten per cent. of the weight of the drug and such a comparatively

large amount of water concentrated in a small volume must materially affect the alcoholic strength of the solvent. Conversely, a fibrous drug will actually absorb water from a menstruum of low alcohol content so that the first portions of the percolate will contain a solvent of higher alcoholic strength than the original menstruum. It is, perhaps, unnecessary to comment upon the possibility that conditions of this sort are almost certain to lead to extensive precipitation in liquid products.

The actual alcoholic strength of the percolate increases in every percolation as the content of extract diminishes and the volume of solvent becomes greater. There has not been, up to the present time, any published determination which shows the regularity of this increase in alcoholic percentage but the fact is well known if too often disregarded. Lloyd has suggested that the solvent power of a partially saturated menstruum is qualitatively different from that of the fresh menstruum; it would be of considerable interest in connection with the problems of percolation if this question were fully investigated.

THE MARC.

With the exhaustion of the drug the process of percolation enters a new phase. The residue within the percolator, however, may still claim attention for it usually contains a quantity of valuable material, especially alcohol. The recovery of this valuable substance properly belongs to the economic side of the process and is highly important. A variety of methods are used for this purpose: the most common procedure and the one which is always applied in large scale operations is the use of a dreg still into which the wet marc is packed and then subjected to the action of live steam which drives off nearly all the alcohol in vapor and this is then condensed by suitable means and collected. About two-thirds of the residual menstruum may be recovered by pressing out the marc in a tincture press but this is neither convenient nor economical for large operations. Washing out or "displacing" the menstruum with water is the process first used by pharmacists[1] to recover the valuable alcohol. Smith[2] has described a percolator which has an ingenious device whereby the apparatus may be reversed and the alcohol floated out of the

[1] *Jour. de Pharm.* 2, 165, 468, (1816). This Journal, Vol. 91, 17, (1919).
[2] *Pharm. Jour.* 18, 291, (1858).

marc on water introduced below and Elborne[1] later advocated the same idea.

As early as 1836, however, the use of water to "displace" alcohol from marcs was questioned by Soubeiran[2] who showed that, contrary to the earlier idea, the displacing water mixes with the alcohol of the menstruum. Indeed it is doubtful whether much more than three-fourths of the residual alcohol can be recovered by this process, for the quantity of water necessary even to approximate a complete washing out of the menstruum is impracticably great and the last portions are too weak in alcohol to allow economical handling. The following case, from the writer's experience, will serve as an illustration. Twelve pounds of coarsely ground drug were moistened, packed, and percolated in the usual way with twelve gallons of diluted alcohol. When the percolator had drained the residual menstruum was displaced with water and the issuing liquid tested from time to time for the presence of alcohol. After thirty gallons of water had passed through the marc the next portion of liquid gave strong evidence of the presence of alcohol. It may be somewhat roughly calculated that, at the end of the percolation, the marc contained six pints of alcohol and that, therefore, forty times its volume of water was insufficient to wash it completely from the drug fibre. In addition to its general inefficiency the practise of washing alcohol out with water is not applicable to mucilaginous drugs like senna, buchu, gentian, or rhubarb which form a gelatinous mass within the percolator as soon as a portion of the alcohol has been removed and this effectually terminates the process.

HOT PERCOLATION.

It is usually possible to hasten the process of percolation by employing a hot menstruum and several forms of apparatus have been devised for this purpose. In general this procedure offers no advantages over the ordinary cold process except shortening the time. Hot solvents, too, frequently dissolve substances which are insoluble in the cold solvent and which are deposited with more or less promptness as soon as the percolate reaches the room-temperature. Alcohol, for instance, dissolves saponins, waxes, hydrocarbons, and phytosterols when hot and deposits them on

[1] *New Remedies*, 9, 323, (1880); from *Pharm. Jour.*

[2] This Journal, Vol. 10, 221, (1838); from *Bul. Gen. de Therapie.*

cooling. If the deposit occurs soon after the percolation the case is sufficiently undesirable but if the insoluble matter does not precipitate for some time or if the deposition is spread over a long period of time it makes an unsightly product which does not redound to the pharmacist's credit.

Percolation with hot water, as, for instance, in the extraction of cascara and of triticum, is commendable and desirable for, with cold water which percolates very slowly and which contains nothing of a preservative nature, molds are quite likely to develop in the wet drug which renders the product unfit for medicinal use.

OTHER METHODS OF PERCOLATION.

One of the prominent characteristics of pharmacists as a class is their ingenuity and this is nowhere more apparent than in the number and extent of the processes which they have devised in the last hundred years for extracting drugs. Since the early apparatus of Count Réal[1] which was the first step in the abolition of the use of the tincture press down to the present time new forms of apparatus and novel methods for percolation have appeared in a continuous stream.

In the case of most of these novelties the words of John U. Lloyd apply with significance, "simple percolation is as yet unexcelled and my experience with complex forms of apparatus has invariably led to their rejection and a return to the simple percolator."[2]

It is my purpose here to consider in detail first the processes which have been applied most widely and then to refer briefly to the less common methods.

REPERCOLATION.

When the price of alcohol rose following the disturbed conditions incident to the Civil War it profoundly affected pharmaceutical practise. Dr. Squibb set himself to the task of finding some method for economizing the use of alcohol in percolation. His first suggestion was that instead of using a large volume of alcohol to extract the weaker portion of a partly exhausted drug, the weak drug should be sacrificed and the alcohol saved, the pharmacist being satisfied with 75 per cent. of fluidextract from 100 parts of drug.[3] Later[4] a similar suggestion was made by F. B. Stuart.

[1] *Jour. de Pharm.* 2, 165, (1816).
[2] *Proc. A. Ph. A.* 1887, 582.
[3] *Proc. A. Ph. A.* 1865, 201.
[4] *Proc. A. Ph. A.* 1888, 250.

This idea was not favorably received however, and, in the next year,[1] Squibb published the details of his process of repercolation, "Improved Process for Officinal Fluid Extract of Buchu," following it with an application to cinchona[2] and, much later, with an extensive study which may well be considered a pharmaceutical classic.[3] In the earlier directions for his process Squibb adopted the customary evaporation of weak percolate; later he revised the procedure so that a fluidextract was obtained directly from the process without evaporating and the weak percolates were preserved and used on the next batch of drug.

DR. E. R. SQUIBB
Originator of the process of repercolation.

At about the same time a similar process was developed in England by R. W. Giles.[4]

The fundamental principle of repercolation is to saturate thoroughly the first fractions of percolate by mixing them as macerating menstruum with fresh portions of the drug. In the revised process, the drug is divided into three or four portions which may be of equal weight or which may decrease in weight from the first to the last to be treated; the first portion is percolated in the ordinary fashion and a definite amount of percolate reserved; a second

[1] *Proc. A. Ph. A.* 1866, 81.
[2] *Proc. A. Ph. A.* 1867, 391.
[3] This Journal, Vol. 50, 209, (1878). *Ephemeris*, 3, 993, (1887).
[4] *Pharm. Jour.* 26, 219, (1866); 33, 521, (1873). *Proc. A. Ph. A.* 1867, 140,

definite amount of percolate is taken and this is used to moisten the second quantity of drug. The remainder of the percolate from the first portion is used to percolate the second quantity of drug. A definite volume of percolate from this second percolation is reserved, the next fraction of percolate used to moisten the third lot of drug, and the rest used to percolate the third lot. The percolate from the third quantity of drug is handled exactly as that from the

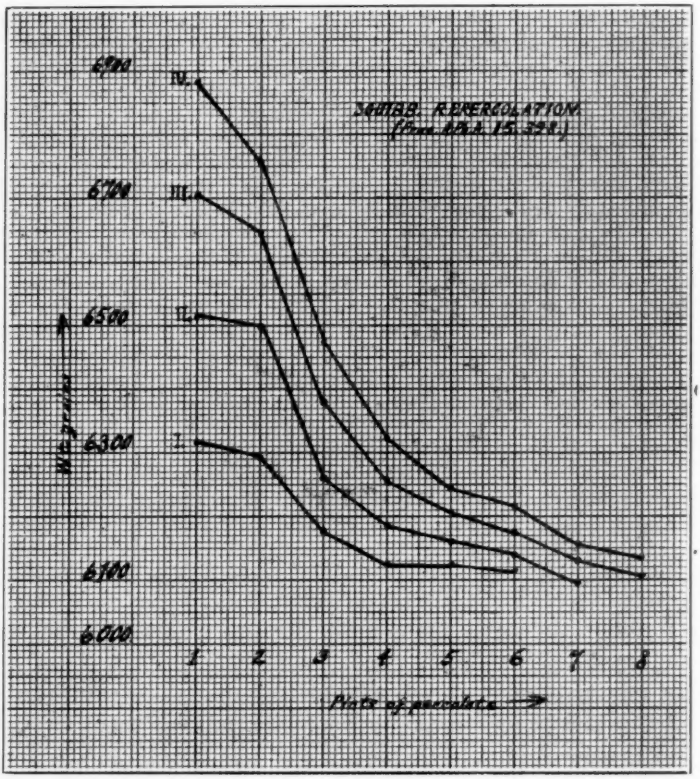


Chart E.

first and second lots and so with the fourth fraction when all the reserved portions are mixed together and used as finished fluidextract the weak percolates from the last percolator being set aside for the next extraction of the particular drug.

Chart E. presents in graphic form the results reported by Squibb in the repercolation of red cinchona by his first process. Four por-

tions of sixteen troy ounces each of drug were extracted in succession; the percolate was collected in fractions of a pint each and weighed. As pint No. 1 from percolation No. 1 becomes approximately pint No. 2 from percolation No. 2 and pint No. 3 from percolation No. 3, etc., the difference in weight between the pints shows the increased saturation due to Squibb's method.

This ingenious process has been subjected to detailed study by many investigators and has provoked much discussion and criticism. Procter[1] protested that the complicated manipulation involved in the process made it unsuitable for the pharmacopoeia. Diehl,[2] who termed it "fractional" percolation, made an extensive study of it with the coöperation of several other pharmacists. He concluded that fractional percolation offers no advantages over the simpler process. The following figures taken from one of Diehl's tables shows the percentage of the total extract which was contained in the reserved portion in the two processes of simple and fractional percolation:

Drug.	Simple.	Fractional.
Taraxacum,	66.43 per cent.	75.00 per cent.
"	83.75 "	82.51 "
Senna leaves	67.95 "	
"	66.80 "	72.79 "
Eucalyptus leaves	62.50 "	75.32 "

Lloyd[3] decided in favor of simple percolation after extensive experimentation; Moore's results show only a slight advantage in repercolation;[4] Arny and Oxley[5] found simple percolation better for gentian; Kelley[6] did not find repercolation satisfactory for gentian, uva ursi, or squill; and Sayre reported it insufficient.[7]

J. W. Colcord, after wide experience with various forms of percolators, concluded that repercolation must ultimately become the official process.[8] Andrews[9] found a slightly modified repercolation

[1] This Journal, Vol. 41, 295, (1869).

[2] *Proc. A. Ph.A.* 1879, 727; 1880, 424; 1878, 681; This Journal, Vol. 41, 337, (1869); *Pharm. Rund.* 7, 25, 60, (1889).

[3] This Journal, Vol. 50, 12, (1878).

[4] This Journal, Vol. 62, 333, (1890).

[5] *Proc. A. Ph. A.* 1910, 1104.

[6] *Proc. Kansas Ph. A.* 1897, 15; *Proc. A. Ph. A.* 46, 683, (1898).

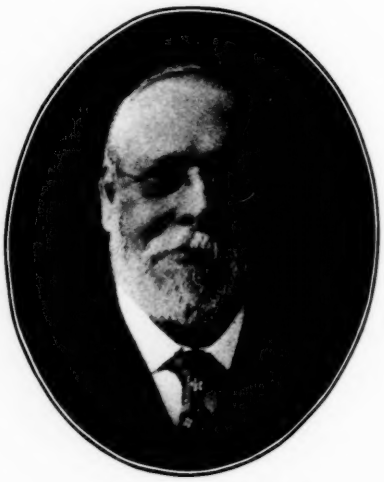
[7] *Drug. Circ.* 1897, 212; *Proc. A. Ph. A.* 1898, 685.

[8] *Proc. Mass. Ph. A.* 5, 170, (1886); *Proc. A. Ph. A.* 1887, 10.

[9] *Pharm. Jour.* 68, 336, (1902).

process suitable for the extraction of alkaloid drugs. Bird[1] approved of the process and Musset[2] recommended repercolation for the preparation of fluidextracts. Scoville[3] stated that repercolation is satisfactory for the extraction of resinous drugs.

In expert hands the process of Squibb gives excellent results with menstrua which do not contain a large proportion of water. In the extraction of those drugs which, like gentian, rhubarb, kino, and phytolacca, yield large quantities of extractive soluble in diluted alcohol the simpler process is preferable but repercolation may



PROF. C. LEWIS DIEHL
A painstaking worker on fluidextracts and the processes of percolation.

be applied to advantage in the extraction of ginger, cimicifuga, ergot, hydrastis, gelsemium, and especially where such solvents as acetone, chloroform, ether, or ligroin are used as menstrua.

INTERRUPTED PERCOLATION.

Interrupted or suspended percolation is the name given to a variation of the ordinary process of simple percolation by C. A. Seifert.[4] The practise in this case is founded upon sound principles

[1] *Pharm. Jour.* 54, 158, (1894).
[2] *Pharm. Centr.* 1897, 862; *Proc. A. Ph. A.* 1898, 681.
[3] *Proc. A. Ph. A.* 1910, 1114. (Discussion.)
[4] *Proc. Calif. Ph. A.* 1892, 123.

and has been approved by many students of extraction. It is based upon the idea of combining maceration with percolation in such a way that every portion of fresh mentruum added to a drug in a percolator shall have as much or more opportunity to macerate the drug as the first portion of menstruum has under the official procedure. As is well known, the early portions of percolate contain the most readily soluble constituents of the drug so that the later fractions of the menstruum encounter the most difficult portions of the extractive to dissolve. The common idea seems to be that the rate of flow of percolate may be accelerated as the percolation proceeds inasmuch as the quantity of extractive is diminishing and therefore does not require as long for solution, whereas the converse is really the true condition.

The principle of interrupted percolation is as follows: The drug is moistened and packed in the usual way and is then macerated for the official period with enough menstruum to "flood it;" at the termination of the period of maceration percolation is begun and a quantity of percolate equivalent to the volume of menstruum first added is collected. Meanwhile fresh menstruum has been added to take the place of that percolated out and, when the first volume of percolate has been obtained, the percolation is stopped and the drug allowed to macerate in the second portion of menstruum. After a certain time percolation is again allowed to proceed until the second menstruum has been percolated out, a third portion of fresh menstruum having been added to the drug. The percolation is again stopped, the drug again macerated, and the procedure continued until the drug is exhausted.

Searby[1] strongly approved this method as also did Edel[2] who claims that the reserved portion in the manufacture of fluidextracts by this method contains more extract than that in the U. S. P. process. J. W. Colcord[3] was also of the belief that alternate maceration and percolation is the best procedure for the extraction of a drug. Seifert shows that interrupted percolation is of especial value with drugs which yield large amounts of extract, as senna or cinchona. With resinous drugs such as ginger, the process did not present any advantage over simple percolation. Seifert reports the following results.

[1] Discussion, *Proc. Calif. Ph. A.* 1892, 125.
[2] *West. Drug.* 1893, 218; 1899, 216.
[3] *Pharm. Rec.* 6, 197,(1886).

TABLE.

	Senna.		Cinchona.		Ginger.	
	S. G.	Per Cent.	S. G.	Per Cent.	S. G.	Per Cent.
Fraction 1	1.025	15.00	0.952	11.66	0.885	25.00
" 2	1.050	22.50	0.976	26.66	0.050	7.50
" 3	1.044	20.00	0.994	28.33	0.842	3.33
" 4	1.036	20.00	1.020	38.00	0.836	1.66
" 5	1.018	16.00	1.010	31.66	0.827	0.83
Finished Fldext.	1.035	18.00	1.000	26.66	0.846	6.66

Seifert does not state the quantities of drug taken nor the volume of percolate collected but inspection of his paper leads to the opinion that he used 1,000 Gms. of drug and collected 200 Mil. portions of percolate. He suspended the percolation for 24 hours between the collection of each fraction of percolate and did not vary this period during the process. His results plainly show the advatages of alternate periods of maceration and percolation.

Many years earlier Alonzo Robbins[1] investigated the effect of interrupting percolation in connection with some other work and his results led him to conclude that no advantage came of it. Robbins, however, did not give the method a fair trial; he shortened the period of maceration as the time went on instead of lengthening it or keeping it uniform and also abandoned the macerating after four periods of maceration. Nevertheless a critical scrutiny of his results show a slight advantage in the interrupted process.

In the same year Lloyd[2] published the results of an experiment on the extraction of cimicifuga by what he termed "interrupted" percolation, proceeding as follows: 24 troy ounces of drug were moistened and packed and, without macerating one fluidounce of percolate was run off. The operation was then suspended and the drug was allowed to macerate for sixteen hours at 100° F. Then seven portions of one fluidounce each were percolated off. The drug was again macerated one day and eight fluidounce portions of percolate were collected. After 32 fractions had been collected the percolate was taken in two-ounce fractions until the drug was exhausted. Results from this experiment are plotted in Chart F. This experiment clearly shows the increased concentration due to the maceration. The idea of combining maceration with percolation was apparently favored also by Squibb for, in

[1] This Journal, Vol. 50, 329, (1878).
[2] This Journal, Vol. 50, 437, (1878).

his description of the well-tube percolator, he says[1] one of the advantages of the apparatus is that it combines maceration with percolation.

In this connection some figures obtained by the writer in the

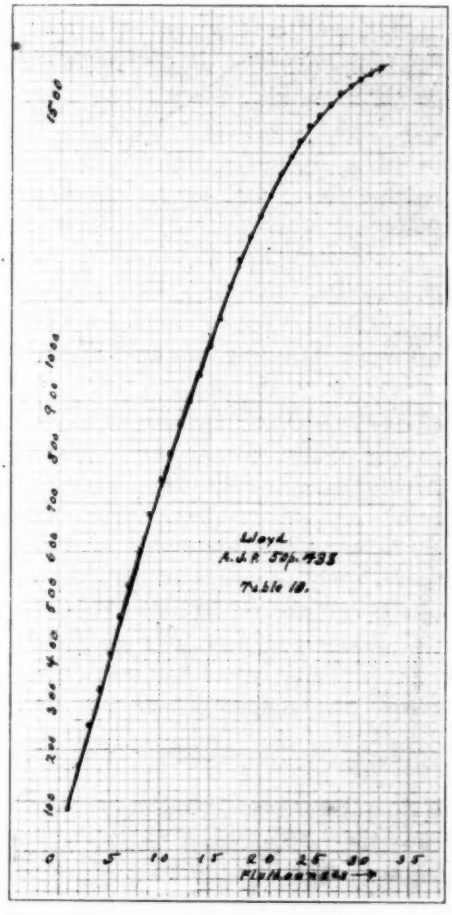


Chart F.

extraction of 16 2/3 pounds of phytolacca are of interest. The drug was moistened, packed in the usual way and macerated with diluted alcohol for two days. Three pints of percolate were then taken, the flow being adjusted to drops. The percolator was shut

[1] *Proc. A. Ph. A.* 1872, 183.

and the drug macerated for four days at the end of which time three pints more of percolate were collected. Then the drug was macerated for six days when a third three pints were collected; the next maceration was for eight days at the end of which time three pints of percolate were run out. The last period of maceration was ten days long and then four pints of percolate were collected. The specific gravities only of the percolates were determined. Below is a tabulation of the results:

TABLE.

Fraction.	Period of Maceration.	Specific Gravity.
1	2 days	0.9853 at 25° C.
2	4 "	0.9848
3	6 "	0.9833
4	8 "	0.9826
5	10 "	0.9657

The specific gravities of the first four percolates were almost identical and this shows a distinct advantage in the process especially when it is remembered that the first portions of percolate usually contain all of the drug moisture and so are of higher specific gravity than equally concentrated solutions, the solvent of which is the undiluted menstruum. The above process occupied 30 days which, it may reasonably be argued, is too long a time to devote to a percolation of this sort. But if one considers the economy of menstruum, the elimination of many details of the other processes, and the quality of the product, this process must be recommended as practicable. At present the writer is using it exclusively in extensive work on the extraction of plants and finds it satisfactory.

METHODS INVOLVING THE USE OF PRESSURE.

From time to time it has been considered advisable for a variety of reasons to hasten the rate at which the precolate passes through the drug by applying extra pressure to the percolation apparatus. A large number of ingenious forms of apparatus have been devised to carry out this purpose. They may be classified in three ways according to the manner of applying the extra pressure. The first class follows the method of Count Réal[1] who contrived a tall column of liquid so that the hydrostatic pressure would act directly upon the surface of the packed drug and some of this class are

[1] *Jour. de Pharm.* 2, 165, (1816).

merely modifications of Réal's apparatus. In this category belong the methods of Wuertzer,[1] Brandes,[2] Beindorf,[3] Rosenwasser[4], Berry,[5] Hallberg's peerless percolator,[6] A. I. Cohen,[7] and of B. S. Procter.[8]

A second class utilizes air pressure applied to the surface of the drug. Pumps of various kinds are employed by Semelbauer,[9] in three forms of apparatus suggested by Romershausen,[10] by Signoret,[11] Allen,[12] Nunn,[13] and by Lenz.[14] Marpmann,[15] Phillips,[16] and Cowley[17] utilize air pressure obtained by the force of a column of liquid acting on an enclosed volume of air. The elaborate method of Duffield,[18] Fairthorne,[19] and Thompson,[20] include exhaustion of the drug, vacuum maceration, and expulsion of the percolate by compressed air.

The third class accomplishes the pressure by applying suction to the bottom of the percolator. Maben[21] employs an ordinary water pump or aspirator; Arthur[22] uses an exhausting syringe, and Platt[23] a Sprengel pump.

It must be borne in mind that any process which employs pressure other than that produced by the natural effect of gravity upon the menstruum is not a true process of simple percolation because

[1] *Rep. der Pharm.* 7, 230, (1819).
[2] *Ibid.* 7, 234, (1819).
[3] *Mag. für d. Pharm.* 9, 185, (1826).
[4] This Journal, Vol. 53, 567, (1881).
[5] This Journal, Vol. 55, 587, (1883).
[6] *West. Drug.* 15, 46, (1893); *Proc. A. Ph. A.* 1893, 383.
[7] Merck's Report, 1899, 4; *Proc. A. Ph. A.* 1899, 383.
[8] *Pharm. Jour.* 36, 641, (1877); This Journal, Vol. 49, 372, (1877).
[9] *Rep. der Pharm.* 3, 88, (1817).
[10] *Ibid.* 6, 316, (1819).
[11] This Journal, Vol. 33, 319, (1861).
[12] *Pharm. Rec.* 7, 6, 66, (1887).
[13] *Pharm. Jour.* 1898, 981.
[14] *Ber. d.d. Pharm. Ges.* 15, 137, (1905).
[15] *Pharm. Centr.* 29, 507, (1888).
[16] *Pharm. Rec.* 8, 213, (1888).
[17] *Pharm. Jour.* 1898, 418.
[18] This Journal, Vol. 41, 2, (1869).
[19] This Journal, Vol. 54, 236, (1882).
[20] This Journal, Vol. 55, 537, (1883).
[21] *Pharm. Jour.* 46, 941, (1887).
[22] *Pharm. Jour.* 49, 850, (1889).
[23] *Pharm. Era*, 1892, 113; *Proc. A. Ph. A.* 1892, 403.

the relationships between the drug, absorbed menstruum, and the precolate are upset when the precolate is driven through the drug. If a drug is suitable for extraction by simple percolation, then a proper regard for the conditions of fineness of powder, moistening, packing, and choice of menstruum will be sufficient to ensure success without any resort to external force. As I have shown above, the idea that the precolate may be hastened through the drug is based upon erroneous notions of the principles of percolation. The ideal condition is such a one that the menstruum is in contact with the drug just long enough to establish equilibrium between the factors present before the liquid drops through the orifice. This equilibrium is not established in any short period of time and, consequently, any process which does not take this idea into consideration is open to pharmaceutical objection. These complex forms of apparatus have uniformly been rejected by pharmacists and the simple percolator still is to be seen in every establishment where drugs are extracted.

MISCELLANEOUS PROCESSES AND APPARATUS.

The following contains a brief chronological account of a number of processes for percolating drugs and making fluidextracts with an indication of the essential feature of each.

The well-tube percolator of Squibb has already been described. The same idea is used in a percolator made of "Appert" glass.[1] Squibb has also described[2] an "automatic" percolator the chief feature of which is an ingenious method for the automatic addition of menstruum to the drug.

In 1858 appeared Bashford's Compound Percolator which is provided with an outside jacket so that it may be operated to allow hot percolation.[3]

N. S. Thomas[4] in 1865 obtained a patent for a method of preparing fluidextracts which consists in moistening the drug with successive portions of the menstruum, macerating, and pressing out in a tincture press after each addition. The operation is continued until the amount of liquid pressed out is equal in volume to the fluidextract which the given amount of drug should furnish. Squibb[5] says the process is an old one.

[1] Remington, "Practice of Pharmacy," 1907, 375.
[2] This Journal, Vol. 30, 97, (1858).
[3] This Journal, Vol. 30, 81, (1858); from the *San Francisco Bulletin.*
[4] This Journal, Vol. 37, 81, (1865).
[5] This Journal, Vol. 37, 182, (1865).

Dursse[1] patented a percolator with a tightly fitting cover which may be adjusted to control the rate of flow of percolate and which minimizes evaporation.

In 1869 Samuel Campbell published his process for the preparation of fluidextracts.[2] Campbell believed maceration to be the most important part of percolation. He used glycerin in his menstrua and macerated the drug for four days after packing it in a glass funnel percolator. After the maceration the drug was percolated until the proper volume of fluidextract was obtained when the operation was stopped and the percolate treated as finished fluidextract. This did away with prolonged percolation to obtain weak percolates which must be concentrated and dissolved in a reserved portion. But Campbell's process did not thoroughly extract the drug. King,[3] Archibald,[4] and Reynolds[5] reported against Campbell's process; A. B. Taylor[6] showed that the idea of long maceration is a good one. Campbell apparently abandoned the process later.[7]

Calvert[8] suggested an apparatus for percolating with very volatile solvents which consists of two "aspirator" bottles one of which is set on a shelf and used as a reservoir for menstruum while the other is inverted and serves as the percolator. The two bottles are connected by tubing between the lower apertures. Menstruum flows from the reservoir into the percolator and the percolate may be collected out of contact with the air.

Taylor has suggested[9] using a portion of the finished preparation from a previous batch to moisten the drug and to start percolation before adding the menstruum. Dieterich[10] describes the Christ-Dieterich percolator the essential feature of which is an inverted bottle of menstruum set into the top of the apparatus to furnish an automatic supply of menstruum.

Arny[11] has devoted much attention to the study of loss of vola-

[1] This Journal, Vol. 41, 384, (1869).
[2] This Journal, Vol. 41, 384, (1869).
[3] This Journal, Vol. 42, 29, (1870).
[4] This Journal, Vol. 42, 117, (1870).
[5] This Journal, Vol. 41, 525, (1869).
[6] *Proc. A. Ph. A.* 1869, 390.
[7] This Journal, Vol. 44, 102, (1872).
[8] This Journal, Vol. 55, 269, (1883).
[9] This Journal, Vol. 55, 556, (1883).
[10] *Pharm. Centr.* 29, 168, (1888).
[11] *Proc. A. Ph. A.* 40, 169, (1892).

tile menstrua in percolation and has described three forms of apparatus designed to minimize this defect. In 1895 Forrest[1] described an apparatus for continuous percolation which consists of a series of percolators arranged so that the percolate from one becomes the menstruum for the next and so percolates through the series. A form of percolator for volatile menstrua was designed by Barnard.[2] The whole apparatus is air tight in this type and a small tube which extends from the receiver up through the drug in the percolator to the inside of the cover serves to convey the air displaced in the receiver to the top of the percolator. Wood[3] suggests a modification of the siphon delivery tube in the well-tube percolator. He arranges a pair of corks in the end of the tube in such a way that the percolate must drop slowly and its flow can be controlled. Phillips[4] described a very simple apparatus for hot percolation.

Barksdale[5] suggested a percolator fitted with a stirring device and operated as follows: the drug is placed in the percolator and a volume of menstruum equal to half the quantity of fluidextract which the drug should yield is poured on the drug. The whole is stirred for at least thirty minutes, allowed to macerate two days, and then the same volume of menstruum is added and percolation started. When the liquid has percolated through enough more menstruum is added to furnish a 75 per cent. reserve (by volume) and then the drug is exhausted by simple percolation and the weak percolate handled according to the official process. It is claimed that the drug is more quickly exhausted by this process than by the official one.

The "double-tube" percolator is an ingenious modification of Squibb's well-tube idea. An ordinary percolator is fitted with a central tube of rather large bore around which the drug is packed in such a way that the percolate flows into the tube. Within this central tube is a smaller tube which extends through the spout of the percolator and is held in place by a cork or rubber nipple.

This inner tube may be raised or lowered to control the height of the menstruum in the drug, the rate of flow and the period of

[1] *Pharm. Jour.* 55, 538, (1895).

[2] Merck's Report, 1899, 220.

[3] *Pharm. Era*, 1899, 359.

[4] *West Drug.* 11, 210, (1889); from the *Pharm. Record.*

[5] *Ibid.* 21, 116, (1899).

[6] Remington, "Practice of Pharmacy," Ed. 5, 1907, 265.

maceration. This is a very convenient form of percolator and is worthy of extended trial. In the writer's experience it has proved well adapted for percolation and especially for interrupted processes. With this apparatus it is impossible to leave the drug accidentally without maceration as the level of the percolate is always as high as the inner tube.

Lloyd's still[1] is an apparatus designed for the extraction of drugs and the concentration of the percolate without the risk of alteration due to heat. The apparatus is complex and the reader must be referred to the treatise issued by Lloyd Bros. for an extended description of it.

A simpler form of apparatus for the preparation of extracts under reduced pressure was suggested by Beard[2] who uses a percolator fitted with a side tube like the larger tube of a Soxhlet extractor and conducts the percolation in a partial vacuum.

PERCOLATION *versus* MACERATION.

Maceration as a process for the extraction of drugs has ever been a rival of the more popular process which supplanted it in 1833. From time to time advocates of maceration rise and attempt to do away with percolation as the official process. Weber,[3] Schmitt,[4] and a writer in the *Répertoire de Pharmacie*[5] have marshalled arguments in favor of the older method. Edel[6] has answered some of these.

It is claimed that the products made by maceration are more uniform and produce less precipitation than those made by percolation, that the process is very much simpler and not so liable to accident in inexpert hands, and that it takes less time.

The advocates of maceration forget that the process of percolation was designed originally to remedy a serious defect in the earlier procedure, namely the fact that a certain proportion of the extract was always retained in the drug and that, therefore, the liquid extract obtained by maceration did not represent 100 per cent. of the drug but only a fraction of that figure. Remaceration,

[1] U. S. Patent No. 777,115. The treatise is known as "The Development of the Pharmaceutical Still," 1905.

[2] *Jour. Am. Pharm. Assn.* 7, 964, (1918).

[3] *Drug. Circ.* 1898, 216; *Proc. A. Ph. A.* 1899, 381.

[4] *Pharm. Ztg.* 49, 102, 291, (1904); *Proc. A. Ph. A.* 1904, 283.

[5] *Proc. A. Ph. A.* 1882, 31.

[6] *West. Drug.* 1899, 57.

to be sure, would recover a large part of this retained extract but this would involve other difficulties which would rob the method of all advantages.

It is admitted that many tinctures may successfully be prepared by maceration and that maceration is more practicable for tinctures of certain resinous drugs than percolation, but for concentrated preparations like fluidextracts where the exhaustion of the drug is to be accomplished with as little menstruum as possible maceration is distinctly a failure. This seems to be the concensus of opinion among American pharmacists.[1]

The following figures[2] show plainly that maceration does not equal simple percolation. 750 Gms. of gentian root were treated with 1950 Gms. of dilute alcohol. One such batch was macerated for four days and pressed out; another was percolated.

	Percolated.	Macerated.
Volume of product,	1005 Mils.	1530 Mils.
Specific gravity,	0.958	0.931
Dry extract,	185 Gms.	174 Gms.
Gm. extract per 100 Mils.[3]	18.40 Gms.	11.37 Gms.

That tinctures made by maceration precipitate less than those made by percolation is hardly true for the majority of causes for precipitation exist equally in both cases. With fluidextracts where factors which induce precipitation are introduced by the evaporation of weak percolate we should expect more of this feature. It is true, however, that in maceration the bulk of the precipitation takes place in the macerating vessel and, therefore, is not as apparent as it is in percolation but it is, nevertheless, as real.

Percolation is unquestionably a more complicated and difficult process than maceration and demands more knowledge of the art of pharmacy from the operator but this cannot be considered a valid argument against the process. We have a right to demand that a pharmacist be familiar with and expert in the processes of his art. Consequently any sacrifice of product quality for the sake of simplifying a method is unjustifiable. The experience of a century has led to the retaining of the process of simple percolation as the best general method for the extraction of drugs.

[1] This Journal, Vol. 61, 187, (1909).

[2] Herzog, *Ber. d. d. Pharm. Ges.* 15, 107, (1905).

[3] These figures added by the writer.

THE PRODUCT.

The product of the process of percolation is the percolate. If this is subjected to any further treatment, with the possible exception of filtration, some other distinct process is involved. The percolate is not, however, in condition for use except in the preparation of tinctures, wines, certain elixirs, or if repercolation has been employed and, consequently, is frequently processed again. Much study has been made of the percolate and the various methods of treatment applied to it and, while this aspect of the subject is strictly outside the limits of percolation, the further treatment of percolates is so intimately connected with the extraction process that no account of the latter would be complete without a consideration of the fate of the product.

In the manufacture of solid extracts the whole of the percolate is evaporated nearly to dryness; for fluidextracts this evaporation is confined to the "weak" percolate which is concentrated only as far as the volume of the reserved portion necessitates. During the evaporation of an alcoholic percolate practically all of the alcohol vaporizes early leaving the extractive in contact with hot water.

The temperature at which the evaporation is conducted may affect the quality of the ultimate product especially in such cases where easily decomposed or rearranged substances are present and particularly in acid liquids. In the latter case it must be remembered that evaporation increases the concentration of the acid and even if it is a weak acid it may become concentrated enough to hydrolyze glucosides and decompose alkaloids.

It is, therefore, advisable to conduct all evaporations under reduced pressure but is not absolutely necessary to do so in every case. A certain amount of hydrolysis and decomposition will occur no matter how carefully an evaporation is conducted even *in vacuo;* indeed, hydrolysis will take place in tinctures of some drugs which have not been subjected to heat at any stage of their preparation.

The changes which take place in the extracted matter during evaporation have been studied but they are of so complicated a nature and involve so many substances about which we know little that our knowledge of this whole subject is only fragmentary. We have merely a superficial idea of the nature of substances as they exist in the living cell and can, therefore, state little about the changes which they undergo in reaching a form in which we may investigate them. I think that much time and energy have been

devoted by pharmacists to a prevention of changes which are, for pharmaceutical purposes, often wholly unimportant. If proteins are coagulated, starch precipitated, carbohydrates caramelized, and non-medicinal tannins oxidized what does it matter? The essential purpose is the preservation of therapeutic value and if this is accomplished the important part of the process is successful.

And that precipitation, oxidation, and other phenomena to which evaporation is liable to lead are not usually fatal the following evidence is offered: Diehl[1] stated that the moderate heat required in the preparation of fluidextracts does not injure them. Maisch was of the same opinion and a fluidextract of Ipecac made by him about 1864 by an evaporation process was analyzed by Lawall in 1897[2] and found to be above U. S. P. strength even after thirty years.

An investigation of the nature of precipitates in tinctures was reported by Cripps[3] who found the following: the deposit in Tr. Calumba contained none of the active principles; that in Tr. Cardamom Comp. was almost wholly calcium tartrate: tinctures of cinchona (B. P.) exhibited precipitates which contained varying amounts of alkaloids in combination with tannoids; the deposit in Tr. Gentian Comp. was starch, gentian sugar, and albuminous matter, that in a concentrated Tr. Ipecac did not contain emetine; a deposit in a tincture of quinine was calcium sulphate; one in tincture of rhubarb contained gummy matters, calcium oxalate, with a little magnesium and chrysophanic acid. It may thus be seen that in a great number of cases a precipitate contains nothing of therapeutic importance. If an active ingredient separates the fault is with the solvent or the associated compounds.

PRECIPITATION IN FLUIDEXTRACTS.

This subject, because of its great importance, has received much attention from pharmacists. Maisch,[4] Lilly,[5] Diehl,[6] Lloyd,[7] and others have given careful consideration to the causes of precipitation.

[1] *Proc. A. Ph. A.* 1879, 727.
[2] This Journal, Vol. 69, 619, (1897).
[3] *Pharm. Jour. Trans.* 43, 483, (1883); This Journal, Vol. 56, 101, (1884).
[4] This Journal, Vol. 31, 113, (1859).
[5] *Pharm. Rec.* 1888, 233.
[6] *Proc. A. Ph. A.* 1878, 681.
[7] *Proc. A. Ph. A.* Vol. 1881, 408, 421; 1882, 508; 1883, 336; 1884, 410; 1885 411; This Journal, Vol. 56, 499, (1884).

Lloyd has said, "I must say that it does not seem probable that we shall ever, by percolation alone, succeed in making a line of permanent fluidextracts from dry plants. The most important of steps then, is to adapt our menstruum so that it may hold in solution the medicinal principles of each plant and thus render the precipitate which forms inert; for the precipitate will follow."

The known causes of precipitation are: variation in the composition of menstrua whereby extracted matter obtained under different conditions is introduced into a preparation; introduction of water by evaporation of weak percolates and addition to the reserve; oxidation of soluble substances with the production of

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Inventor of the Lloyd extraction apparatus; author of valuable papers on the precipitates in fluidextracts.

insoluble matters: changes of temperature; chemical changes within the solution; the presence of inorganic matters; the presence of minute particles of insoluble substances which at first are invisible but later agglomerate and cause a deposit. It has been shown that light does not cause precipitation.

An interesting effect of precipitation was observed by Lloyd.[1] He found that there is considerable difference between the alcoholic content of a freshly prepared fluidextract and the same preparation after it has precipitated. In the case of Fldext. Podophyllum the change was from 53 per cent. to 65 per cent., in Jalap, 83 per cent.

[1] *Eclectic Med. Gleaner*, 3, 505, (1897); This Journal, Vol. 80, 39, (1908).

to 98 per cent., Eriodictyon from 77 per cent. to 86 per cent., Grindelia, 83 per cent. to 90 per cent. so that a fluidextract which has precipitated will show, on analysis, a larger percentage of alcohol than is declared on the label.

CONCLUSION.

We have now considered every phase of the process of percolation beginning with the apparatus and continuing with a discussion of the drug and its preparation for percolation and an analysis of the mechanism of extraction to an account of the various improved methods and apparatus suggested during the past hundred years.

Some new ideas and certain novel ways of regarding different aspects of the subject have been presented and a portion of these, at least, are at variance with current notions.

The whole survey emphasizes the need for more investigations of the process of percolation and particularly investigations in which the time-factor is not ignored. It is recommended that Colleges of Pharmacy might well include some of this work in their courses on the practise of pharmacy especially with advanced students, many of whom would welcome an opportunity to contribute to our knowledge. In addition to its considerable educational value, such an arrangement would furnish us with a great mass of data our supply of which is to-day very meager.

One of the chief reasons for writing this paper has been a desire to direct attention to and stimulate investigation of the many problems of percolation which still await solution.

SUMMARY.

A general survey of all our published knowledge on the subject of percolation has been made. This knowledge has been classified, coördinated, and subjected to critical analysis. The results of every important contribution are presented and the best technique under varying conditions, as determined by the experience of the whole body of pharmacists, stated.

Certain factors which bear on the problems of percolation and have not yet been investigated are discussed and attention is directed to other factors which require reinvestigation owing to the inadequateness of our present data.

Explanations for a number of phenomena observed during percolation are offered and a discussion of the mechanism of extraction is included.

A section of this survey deals with the various processes and forms of apparatus designed to solve some of the problems of simple percolation, especially such methods as repercolation and interrupted percolation.

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REVIEW OF TESTS FOR METHYL SALICYLATE IN OILS OF GAULTHERIA AND BIRCH.*

By Charles H. LaWall, Ph.M.,

PHILADELPHIA, PA.

Periodicity is one of the commonest of natural phenomena. Man having caught the spirit of nature follows close after in this respect, hence the common adage about history repeating itself. This is particularly true of certain lines of scientific investigation. A particular instance is that of the tests for distinguishing between oil of gaultheria, oil of birch and methyl salicylate, and of detecting mixtures of these oils, for which a new method is published every few years. The reason for this search is found in the wide difference in price and the temptation to mix them or substitute one for the other.

There are certain fundamental factors in a problem of this kind which point to the probability of a test being devised for distinguishing the pure oils, but an equal improbability of any infallible method being discovered of detecting admixtures of one with the other, even in large amounts. In support of this belief let me state my reasons:

Without going fully into the chemistry of the respective oils, it will suffice to say that the differences between them are essentially as follows:

(1) Methyl salicylate is a distinct chemical entity and appears upon the market as such in a state of high purity.

(2) Oil of gaultheria consists of methyl salicylate to the extent of 99 per cent., the balance consisting of a paraffin, an aldehyde, a ketone, an alcohol and an ester.

(3) Oil of birch consists of methyl salicylate to the extent of over 99.5 per cent., the remaining trace consisting of the paraffin and ester, but not the alcohol nor aldehyde.

* Read at the October meeting of the Philadelphia Branch of the A. Ph. A.

It is certain in the light of the foregoing premises that any distinguishing tests must be based upon differences due to the traces of associated substances in birch and gaultheria oils, respectively, for the methyl salicylate factor is common to all three products.

It likewise follows that there is absolutely no hope of any test for detecting added methyl salicylate in either oil of birch or oil of gaultheria by a positive reaction if the methyl salicylate be pure for pure methyl salicylate reacts similarly whatever its origin.

Any possibility of distinguishing these oils, therefore, must be based upon the discovery of a test which will identify these elusive factors which are present in scarcely more than traces in oils of birch and gaultheria, respectively, and to detect mixtures it would be necessary to discover a method which can be transformed into a quantitative reaction or one in which advantage can be taken of its intensity.

The only reactions of a distinguishing nature likely to be discovered are color reactions, and as color reactions are usually uncertain and when translated into colorimetric methods for quantitative use, are rarely very accurate, the chances of accomplishing anything of real value in this research are seen to be very remote, for it is only of academic importance to be able to distinguish the products in a state of purity if mixtures of one with the other cannot be detected with certainty.

From time to time investigators have pursued this *ignis fatuus* of a color reaction which should serve both as a distinguishing test of the pure substances and a method of detecting admixtures, completely ignoring the fallacy of such a quest.

In 1913, Stanislaus and Semmel, in the *Proceedings of the Pennsylvania Pharmaceutical Association*, proposed several reagents for accomplishing this result. The reagents consisted of nitric acid, sulphuric acid and formaldehyde mixed in several combinations. The resulting color reactions with the three products were described as brown, light brown and yellow; straw, light straw and light yellow; amber, yellow and colorless. There is not enough distinctiveness about tests giving such results to make them worthy of consideration as affording hope of detecting mixtures.

In 1914, Watson and Sayre, in the *J. A. Ph. A.*, p. 1658–9, proposed several tests. One was based upon differences of color produced in the three products by sulphuric acid. The reactions are described as dark red, yellow or light red, and colorless for oils

of gaultheria and birch and methyl salicylate, respectively. Assuming that the pure products give these reactions, the chances of detecting methyl salicylate in either of the natural oils would be very slight even if large amounts were added. Another reaction proposed by these authors is based upon colors produced by a mixture of sulphuric acid and an alcoholic solution of heliotropin. The reactions produced in gaultheria, birch and methyl salicylate, respectively, are crimson, less intense crimson and yellow. It is obvious that the same criticism applies here as to the previously mentioned test with regards to the possibility of its being applied quantitatively even in an approximate manner. Still another test proposed by these same authors is applied by adding, successively, sulphuric acid and a saturated aqueous solution of chloral hydrate. With this test the color reactions are more distinctive. The gaultheria gives a green color, the birch a violet, while methyl salicylate gives no color.

I have found this test to give very satisfactory results when some pure samples of the respective products are used, but with mixtures there is no quantitative distinctiveness about the test, the shades of color being influenced more by slight variations in the proportions of the reagents than by differences in the amounts of the respective oils, and the hope that the authors express, that the test may be made quantitative, has not been substantiated by any subsequent work done by the authors of the test themselves or by any other worker who has published his results, although four years have passed since the test was first published.

In 1914, F. C. Umney (*Perfumery and Essential Oil Record*, p. 60) published a test which has been widely quoted and frequently used, as follows:

"To five drops of the oil in a test-tube add five drops of a five per cent. alcoholic solution of vanillin and 1 Cc. of alcohol. Shake well and add 2 Cc. of concentrated sulphuric acid and mix thoroughly." Oil of gaultheria by this test is reported to give an intense crimson color; oil of birch a reddish brown and methyl salicylate a yellow color.

This test is subject to the same defects as some of those previously criticised, in that the methyl salicylate reacts negatively and very large amounts must be added before one can state with certainty that the sample is not pure. It certainly does give a distinctive reaction with some specimens of gaultheria oil.

It is not a difficult matter to devise new tests which appear to give distinctive results working with a single set of authentic samples. I have discovered several such tests in the short time with which I worked in the preparation of this article. It occurred to me that inasmuch as both gaultheria and birch oils are made from drugs which contain more or less woody cellular tissue, that conditions would be favorable for the production of furfuraldehyde in the distillation of these oils, and it will be noted that an aldehyde has been reported in gaultheria oil, although its identity was not established. The application of several of the better known tests for furfuraldehyde, notably the aniline acetate test, such as is used for detecting invert sugar in honey, were applied and, as was expected, positive results were obtained. With this test, for instance, a specimen of authentic gaultheria oil gave an immediate intense red color; birch oil gave a pronounced red color, more slow in its appearance, and methyl salicylate gave a negligible reaction. Other tests for furfuraldehyde, as, for example, the Badouin test for sesame oil, in which hydrochloric acid containing one per cent. of sugar is the reagent, also showed differences in the intensity of the reaction, but when applied to mixtures the test becomes practically valueless, for reasons explained in connection with several of the foregoing tests. It would be easy, also, to defeat the objects of such a test by the addition of a small amount of furfuraldehyde to the methyl salicylate used for adulteration purposes.

At times during the past five or six years it has been stated in print (Schimmel's Report, April, 1914, p. 99) or the rumor has circulated throughout the essential oil trade that the U. S. Department of Agriculture chemists are in possession of a test which enables the detection of adulteration of gaultheria or birch oils with methyl salicylate with certainty. Such test has never been published and if it exists it is probably based upon one of the previously published tests or upon some such reaction as the one I have described for furfuraldehyde, for instances might be found of adulteration so gross, say 90 per cent. of methyl salicylate to 10 per cent. of the genuine oil, that a difference in intensity could be noted. It is more likely that the majority of the prosecutions which have been brought for adulterations of this kind have been based upon inspectors' actual knowledge of admixture.

I have at various times been presented with so-called authentic samples of oils of gaultheria and oil of birch. Three of these sam-

ples possess the negative optical rotation required of gaultheria oil by the U. S. Pharmacopœia. Applying all of the color reactions so far described in the literature of these oils the variations in effect are so marked as to impel the conclusion that there is not likely to be a test which will give uniform results with all authentic samples.

Only one of the three laevorotatory oils gives positive results with Sayre and Watson's chloral hydrate test, and this same sample is the only one which gives positive results with Umney's test. If one relied upon the U. S. P. tests alone they would all pass. Are we to infer that the laevorotatory power is not distinctive of gaultheria oil?

I believe the answer to this question and the explanation of all other inconsistencies in these color reactions is that they are only satisfactory with some samples distilled under certain conditions, and that no test has ever been subjected to the searching application of many authentic samples.

Inasmuch as clinical experiments on the part of investigators working on behalf of the American Medical Association have declared that the natural salicylates have no therapeutic advantage over the synthetic salicylates of equal purity and not one observer in ten can distinguish between unlabeled samples of oils of gaultheria birch and methyl salicylate as regards odor, the final conclusion is: What's the Use? Let's work on something worth while.

Department of Pharmacy,
Phila. College of Pharmacy and Science.

THE PHARMACEUTICAL PLANT CHEMICAL SOCIETY.

By Geo. E. Ewe,

PHILADELPHIA, PA.

A Chemical Society organized among the employees of a plant yields the same primary benefits which surround membership in a nationally organized Chemical Society. Among these benefits may be mentioned, mutual exchange of valuable information; mutual sympathy and assistance in the solving of difficult chemical problems; coördinated effort on chemical matters in general, and social features.

The Plant Chemical Society, however, yields additional benefits:

It acquaints each member with the character of the work being performed by each of the other members, thus leading to teamwork.

It affords a forum for the open and unbiased discussion of technical misunderstandings which are hindering the progress of the work of the plant.

It affords an opportunity to the management of announcing and explaining innovations, thus securing the coöperation of the members and eliminating the normal antagonism to innovations put into operation without explanation.

It affords to both the management and employees the opportunity of presenting and discussing new policies which will advance the work and the prestige of the plant, or discussing existing policies which are hindering the work or damaging the prestige of the plant.

It affords the opportunity of issuing and explaining general instructions on a wholesale plan, thus conserving the time ordinarily expended by the individual discussions and explanations by letter or conference which usually follow the issuance of general instructions on an individual plan.

It affords an opportunity to the member to present his opinions regarding faults in products and processes and to present suggestions for the elimination or correction of the faults.

It affords an opportunity for the members to become better acquainted with each other socially, with the result that mutual sympathy and regard is engendered.

The final and desired result of the Plant Chemical Society is to increase the interest of the member in the scientific aspect of the work of the plant. The importance of this result is attested by the fact that only an interested employee is satisfactory to the highest degree.

In April, 1914, a Chemical Society was established in the plant with which I am connected and the success of the movement has been so thoroughly proven, that I feel warranted in offering an explanation regarding the methods employed in the establishment and conductance of the Society, for the guidance of those plants in which no similar organization is conducted at present.

The plans upon which the Society was organized and is being conducted are, no doubt, capable of improvement, but, nevertheless, have yielded eminently satifsactory results.

The general statement of the aims and purposes of the Society which was presented for the consideration of the Charter Members at the initial meeting read as follows:

AIMS AND PURPOSES OF THE ..... CHEMICAL SOCIETY.

Benefit to the members by reason of knowledge imparted and ability increased through the activities of the Society; especially regarding chemical and analytical chemical matters.

To give to the members, in some degree, a post-graduate course in the chemistry pertaining to the plant.

To give to the members practice in the accurate reporting of results of chemical work.

To increase active interest in the scientific aspect of the work being performed by the ..... Co.

To acquaint each member with the work being performed by each other member.

To invite discussion of ways and means of best performing the chemical work of the plant.

To propagate mutual assistance in solving difficult chemical problems.

To discuss any matter which may prove of value to the members of the Society, if considered worth while by the Chairman of the Society.

This statement of aims and purposes was unanimously adopted and has operated satisfactorily to this date, without amendment.

The rules for eligibility to membership are very broad and read as follows:

RULES FOR ELIGIBILITY TO MEMBERSHIP.

Any employee, preferably possessing chemical training and experience who can contribute to the benefit of the members, or who can be benefitted by becoming a member of the Society, may be a member.

A striking feature of the membership of this Society has been the number of nationalities represented. At various times, the Society has had the honor of having members originally emanating from Italy, China, Russia, Japan, Denmark, France, Holland, Roumania, Cuba, Austria and Germany. Thus the benefit of very many different viewpoints has been obtained upon the subjects under discussion.

MEETINGS OF THE SOCIETY.

The meetings of the Society are held in the Research Department between four and five P.M. on any Friday, except holidays, whenever sufficient matters are in the hands of the Chairman to warrant a meeting. These meetings are called by the Chairman.

The Company, with which I am connected, has recognized the mutual advantages to be derived from membership in the Society and has granted permission for attendance at meetings held during working hours.

OFFICERS OF THE SOCIETY.

At present only two officers are required, namely a Chairman and a Secretary. The Chairman is chosen by nomination and election at a regular meeting and then appoints the Secretary. The Chairman and Secretary hold office for three calender months.

As a rule, the Secretary is nominated and elected as Chairman to succeed his retiring Chairman. The present arbitrary plan of choosing a Chairman and Secretary is based upon length of service with the Company, so that each member has the privilege of becoming Secretary and then Chairman in turn. This plan is not absolutely rigid, as reservation is held that appointment of an indesirable Secretary is not obligatory. However, to date, this plan has been followed without a break and with undoubted satisfaction.

The duties of the Chairman consist of collecting material for meetings, calling meetings, presiding at meetings, and appointing his Secretary.

The duties of the Secretary are to assist the Chairman in every possible way, take up the duties of the Chairman, when the Chairman is unable to functionate, record minutes of each meeting and read at each meeting the minutes of the preceding meeting.

QUORUM NECESSARY FOR HOLDING MEETING.

The quorum necessary for holding a meeting was adopted as being one more than half the membership.

It might be well to note here that at no time, has it been impossible to obtain a quorum, when a meeting was called. No intimation of coercion is exercised to secure attendance at the meetings. The members appreciate the advantages to be derived from attendance. Every effort is made to make the meetings interesting and in order to accomplish this purpose, the practical, rather than the theoretical,

side of subjects is given preference, as it has been found to yield the best results. However, the theoretical side has not been neglected. Only a very few members have shown a lack of interest, chiefly due to inappreciation of the advantages to be gained from the subject matters of the meetings.

RELATION OF SOCIETY TO NON-MEMBERS.

On 5/22/14 it was unanimously decided that contributed papers and other information, when suitable, be presented to other chemical and pharmaceutical societies. Also, when the papers, etc., concern employees of the Company, who are non-members, that the papers, etc., be brought to the attention of these employees.

ORDER OF BUSINESS OF MEETINGS.

The order of business of meetings has gone through a series of changes, designed to accommodate it to the present needs of the Society and at present has the following form:

Call to order.
Reading of minutes of preceding meeting.
Old business.
Reading of contributed papers and notes.
New business.
Installation of new members.
Reading and disposal of correspondence.
Committee reports.
Announcement and discussion of changes and proposed changes in products and processes.
Announcement and discussion of new products and processes.
Miscellaneous announcements.
Reporting and discussion of items of daily work which are of general interest.
Election of officers (when in order).
Announcement of nature of chief business of next meeting.
Adjournment.

A brief discussion of some of the items of the order of business may prove of interest in indicating the purpose and value of these items.

The contribution of papers and notes to these meetings induces to a more thorough performance of certain tasks included in the daily work upon which these papers and notes are based. The member is encouraged to so perfect and round out his work that a

conclusive, interesting and readable report results. In some cases, special arrangements are made to assist the members in doing this. These arrangements include the providing of special materials, books and apparatus and the granting of freedom from usual tasks in order to provide the time for the work. This item of "order of business" has developed into one of the most successful activities of the Society. The papers and notes presented at the meetings total over two hundred for the six years of the existence of the Society. Most of these papers and notes consisted of proved suggestions for economy in labor and materials, the prevention and utilization of wastes and improvements in the products manufactured by and processes used in, the several Departments of the Company represented in the membership of the Society. Some of these papers were publishable and were published and others which carried suggestions which were of value to Departments of the Company which were not represented in the Society were presented to the consideration of these Departments accordingly.

The following list of titles of a few of the papers and notes presented at these meetings will indicate both the scientific and practical interest shown by the members of the Society in the business of the Company:

"The Assay of Tablets Containing Calomel and Calomel and Sodium Bicarbonate."

"Soft Gambir."

"Some Criticisms of (a Product Marketed by the Company)."

"The Determination of Potassium in Colloidal Silver Preparations."

"Standard for Dried and Powdered Magnesium Sulphate for Use in ....."

"The inconsistency of designating (a Product Marketed by the Company) as an Elixir."

"The Taking of Samples for the Chemical Laboratory."

"Improvements in the Manufacture of Emetine Bismuth Iodide."

"The Assay of Creosote Tablets."

"The Duties of an Analytical Chemical Laboratory Connected with a Pharmaceutical Manufacturing Plant."

"The Time Required by Rennin for Coagulation of Milk is Inversely Proportional to the Amount of Rennin Employed."

"Uses of Centrifuges in the Analytical and Chemical Laboratories."

"Some Crude Drug Adulterations."

"The Substitution of Sodium Salts for Potassium Salts in Medicinal Preparations."

"Proportion of Cephaeline in the Market Quality of Emetine Hydrochloride."

"The Pharmacy and Manner of Use of Tethelin."

"Non-Secret Versus Secret Remedies."

"Labeling Practices."

Etc., etc., etc.

The item of "reading and disposal of correspondence" gives to each member the privilege of leading letters received by him which are of interest to the members in general. Letters to the Society are read and their disposal decided upon.

The item of "announcement and discussion of changes and proposed changes in products and processes" includes all types of processes in which the pharmaceutical chemist has an interest, such as processes for the manufacture of products and for the analytical, chemical, botanical, physiological and physical control of the manufacture of products. This item affords a very wide scope for the activities of the individual members and yields many suggestions for improvements in products and processes.

The same is true of the item of "announcement and discussion of new products and processes." The new products and processes are discussed in detail, and the opinions of the "chemical brains" of the Company are obtained upon these matters.

Under the item of "miscellaneous announcements," such information as the acquisition of new literature, changes in personnel, the activities of competitors, forthcoming meetings of outside societies, inter-departmental instructions, etc., are announced and discussed. This item of the "order of business," as mentioned before, affords the opportunity of issuing general instructions, thereby saving the time which would be required for individual instruction and also affords an opportunity for explanations and discussions of instructions, thereby giving all the members the benefit of the explanations at one time.

The principle purpose of the item of "reporting and discussing of items of daily work which are of general interest" is to give the members the benefit of the knowledge gained by each other in their daily work. This item injects a great deal of interest into the daily work since it is the ambition of the members to report at the meet-

ings, some information of general interest he has gained. The Chairman of the meeting develops the importance of this item by editing the daily reports of each member before the date set for a meeting and suggesting to the member the submission of the interesting items in his reports. This item also affords the opportunity to each member to present his technical difficulties and obtain the opinions and help of the other members of the Society in solving the difficulties.

The item of "announcement of chief business of next meeting" affords the members the opportunity of announcing the titles of papers which they intend to present at the next meeting. Subjects for discussion or explanation may also be announced.

As evidence of the true scientific and practical interest developed by the Society, a copy of the minutes for the meeting held on 11/31/17 is herewith reproduced:

MINUTES OF THE 11/31/17 MEETING OF THE ..... CO. CHEMICAL SOCIETY.

Meeting called to order at 4.05 P.M.

Minutes of preceding meeting were read in abstract and approved.

Old business: None.

Reading of contributed papers and notes: Note: "The Instability of (a Certain Commercial Preparation)." Paper: "The Emulsification of Liquid Petrolatum by Lanoline." Paper: "Emulsions of Liquid Petrolatum."

New business: Meeting room arrangements discussed.

Installation of new members: None.

Reading and disposal of correspondence: Several letters were read.

Committee reports: No committees out at present.

Announcement and discussion of changes and proposed changes in products and processes: The transfer of (a product marketed by the Company) to the list of products made extemporaneously upon order. Specific analytical chemical tests adopted for the selection of Glycerin for (a product marketed by the Company). Improvement in methods of manufacture and analysis for mercury in (a product marketed by the Company).

Annnouncement and discussion of new products and processes: The addition of (a product marketed by the Company) to our list

of products was announced; its method of manufacture and standardization was discussed.

Miscellaneous announcements: Several inter-departmental instructions. Meetings of the American Chemical Society, the American Pharmaceutical Association and Franklin Institute were announced; and also subjects to be considered at the meetings. The acquisition of several scientific books was announced.

Reporting and discussion of items of daily work of general interest: A large number of such items were reported and discussed. Among the items might be mentioned: "The application of emulsions of liquid petrolatum to the production of lipovaccines;" "The absence of Oil of Savin from the market;" "The size of samples submitted to the Analytical Department;" "Kieselguhr and Fuller's Earth as adsorbents of alkaloids;" "Some criticisms of U. S. P. tests;" "Conservation in the use of crucibles;" "Results of experiments on optimum temperature of drying (a product marketed by the Company) in order to hasten its manufacture;" "Traces of lead in zinc oxide and their effect on the human economy;" "A white product can be obtained by recrystallizing (a product marketed by the Company) from alcohol;" "Results of experiments to hasten drying of (a product marketed by the Company) by substituting other diluents for that now employed;" "The preparation and uses of Ammonium-Ricinol-Sulphonate;" "The deterioration noted upon compression of rennin tablets and measures required for the manufacture of standardized rennin tablets."

Election of officers: Not in order.

Announcement of chief business of next meeting: Papers on "The Manufacture and Pharmaceutical Uses of Cephaeline," and "The Determination of Chloral Hydrate in (a Product Marketed by the Company)," were announced. The subject of "Methods of Hastening the Washing of (a Product Marketed by the Company)" was announced for discussion.

Adjournment: Meeting adjourned at 5.05 P.M.

Conclusions: The aims and purposes of this Society have been amply fulfilled; the members have received the combined experience of the entire membership; the interest of the members has been enlisted in the solution of difficult technical and scientific problems; the members have received instruction in many subjects, allied to the work, with which they would not otherwise have come into contact; the quality of the chemical work of members has been im-

proved; products and processes have been elaborated and improved; practice in the accurate reporting of results of chemical work has been attained by the members; mutual understanding has resulted from the personal contact and discussion at the meetings, and "esprit-de-corps" has been furthered.

The chief purpose of this communication is to bring to the attention of Pharmaceutical plant operators the idea of conducting a Chemical Society in connection with the plant and to point out the benefits to be derived thereform.

The general plan of the establishment, aims and purposes and conductance of a Pharmaceutical Chemical Society, as outlined above, is entirely amenable to improvement and further development. It is not offered as rigid and unalterable but can be rearranged, abstracted from or added to to meet the demands or desires of any particular plant.

PHARMACEUTICAL RESEARCH LABORATORY,
H. K. MULFORD COMPANY,
PHILADELPHIA, PA.

WOOD ALCOHOL NO LONGER: HEREAFTER METHANOL.*

BY CHARLES BASKERVILLE,
COLLEGE OF THE CITY OF NEW YORK, NEW YORK, N. Y.

Wood (methyl) alcohol poisoning is an unique problem in that it involves not alone physiological changes and technical matters having to do with production and distribution of the toxic agent, but sociological factors as well.

The "adiophorous" spirit obtained by distilling wood (Boyle, 1661) was thought by Taylor (1812) to be a new kind of *ether;* in fact, he called it "pyroligneous aether." Dumas and Peligot (1835) established its resemblance to ethyl (*ether*) alcohol and named it methyl alcohol from the Greek μέθυ mead and ὕλη wood. In fact it may be recalled that the word *alcohol*, derived from the Arabic, *Al Kohl*, at one time meant a fine powder and only later meant spirits.

Commercially the destructive distillation of hard woods (refuse) is the main practical method followed for the production of methyl

* Presented at the 59th Meeting of the American Chemical Society, St. Louis, Mo., April 12 to 16, 1920. Reprinted from the *Journal of Industrial & Engineering Chemistry*, September.

alcohol in America, although in Europe it has been obtained from peat and as a by-product from vinasse, and in the manufacture of wood pulp by a soluble sulfite process. The numerous synthetic methods known at present are too costly to be practiced on a commercial scale. The condensed tarry and acid products distilled from wood are subjected to partial purification by distillation. This crude material, about 80 per cent. pure, is then usually shipped to centrally located refineries in tank cars, drums, or barrels for further purification and rectification.

This crude wood alcohol, "wood spirit," "wood naphtha," a vile-smelling, greenish yellow to dark brown, nauseous liquid, is a complex mixture containing a variety of impurities. They are removed in the main in the first refining, yielding a product containing about 95 per cent. methyl hydroxide. In 1890 processes for greater refinement were put into operation, so that about 1906 a deodorized product (97 to nearly 100 per cent.) was placed upon the market in the United States under such names as "Columbian Spirits," "Eagle Spirits," "Hastings Spirits," "Colonial Spirits," "Manhattan Spirits," "Union Spirits," and "Lion d'or;" in Canada as "greenwood spirits," and "standard wood spirits;" and in Germany in 1912 as "pro spirit." Technically it was called methyl hydrate, carbinol, methylic alcohol, methyl hydroxide, and methanol. The pure substance is a colorless, mobile liquid, having a pure vinous odor, similar to that of pure ethyl alcohol, and possesses a burning taste.

These facts of names and their meanings are not known by all technical men. They are even less known to the "man-of-the-street;" but the layman does know that "alcohol" is the stuff which makes drunk come; that it is the stuff that cheers when downhearted; that uncontrolled it has been a curse in the world; that it is the "real thing" in the disguise of beer or light wine, which formerly rested him when the arduous day's work was done. So when he sees the can or vessel with the label "alcohol" on it, and as he knows "alcohol" is the thing that gives the "kick," rest, or cheer, without considering the qualifying words "wood," "methyl," or what not, he is going to take it. He is little deterred by the "poison" label, for he has a more or less similar idea from the pictures of intemperance, and still he drank. Therefore, the term *alcohol* should cease its present significant use, at least in chemical literature. Technically, all alcohols should become known as "-ol" bodies or

hydroxides, as "methanol," "ethanol," "propanol," "butanol," etc.; methyl hydroxide, ethyl hydroxide, propyl hydroxides, etc.

In 1906 after a vigorous campaign the United States followed England, France, Germany, and other European countries by enacting laws permitting the general use of a tax-free domestic alcohol for industrial purposes, and for light, heat, and power.[1] This law has made us a self-contained nation in regard to certain medicinals; ether, ethyl chloride, chloral hydrate, nitrous ether, and numerous synthetics may be mentioned in illustration. To emasculate alcohol, as it were, the law requires that tax-free alcohol for use in the arts and industries shall have first mixed with it (under close supervision) substances which "destroy its character as a beverage or render it unfit for liquid medicinal purposes." On account of its poisonous properties, difficulty of removal from the resulting industrial alcohol, non-interference with many of the industrial purposes for which the denatured product was intended, and a desire to avoid the destruction of the methyl alcohol business, for methyl alcohol was cheap at that time, the first act designated it as a denaturant, and the Commissioner of Internal Revenue selected it as the principal one.

Up to date some forty-one formulas for "specially denatured alcohol," to be used for designated purposes only, have been authorized under the several acts. Five formulas for "completely denatured alcohol," which may be used for light, heat, and power, have been authorized. One of each of these has been revoked.

The control of the former class (special) is so complete, involving as it does the moral character of the users, that little danger attends its use. One formula (No. 30) allows the addition of as much as 10 per cent. of the purest methyl hydroxide, but its use is restricted to general chemical and physical laboratory purposes.

The latter class (completely denatured) promises some needed relief for the liquid fuel shortage and may consume much the largest portion of denatured alcohol. That means denatured alcohol will become even more common that it is now.

Data collected prior to 1918 indicated that the drinking of liquids containing methyl hydroxide was responsible for many deaths and acute cases of blindness.[2] The "deodorized" methanol

[1] Act of Congress, June 7, 1906; amended March 2, 1907; Act, October 3, 1913.

[2] See extensive report to the New York State Factory Investigating Commission. 1913, by the author.

resembles pure ethanol so closely that the ordinary layman can hardly distinguish the difference between the two. In complex mixtures, whisky, etc., its detection involves very careful chemical analysis. Formerly it cost less than ethanol, so unscrupulous people were tempted to use it as substitute for ethanol in adulterating whisky, essences, extracts, bitters, washes, liniments, balsams, perfumes, etc. The victims were generally those who indulged in the commoner forms of whisky, rum, and wine, although persons not addicted to the use of intoxicating drinks were undoubtedly often affected innocently from drinking Jamaica ginger, lemon extract, essences, bitters, medicines, etc., whose chief menstruum was "deodorized" wood alcohol. At one time the poorer negroes in the Southwest drank it under the name of "white horse" or "old mule." Happily, the abuses grew less through the operation of the National Pure Food and Drugs Act of June, 1906. However, during the penumbra of prohibition many cases of blindness and death occurred through the drinking of wood alcohol or denatured alcohol.

The "completely denatured alcohol" is the more readily obtainable. Formula No. 1 called for 10 per cent. of specified commercial methyl alcohol with one-half of 1 per cent. of approved benzine. This has been, and is, used in radiator water of motor vehicles to make a non-freezing mixture. This may account in part for the cases traced to garages. After the outbreak referred to, this formula was revoked December 29 last, appearing in orders issued January 8, 1920. Hereafter no completely denatured alcohol containing more than 2 per cent. methanol will be allowed. As alcohol of strengths above 80 per cent. require dilution before drinking, it is doubtful if any future acute cases may be attributed to denatured alcohol, that is, after the present outstanding stocks under Formula No. 1 are used up.

However, we cannot be so hopeful in regard to chronic cases culminating in blindness or defective vision which may be attributed to drinking diluted denatured alcohol containing methanol. The denaturing deterrents are selected primarily on account of the nauseous odor and repulsive taste, rather than physiological action. These odors and tastes repel some people. "Rot gut" whiskies and some "mountain dews" are not far behind varieties of denatured alcohol in odor and taste. With added flavoring, denatured alcohol containing 2 per cent. of methanol may be diluted until it contains 1 per cent. or less of methyl hydroxide, and be drunk. Death is

not to be expected, immediate nor early blindness, from such a draught. And therein lies the danger, so apparent to all who are familiar with the cumulative action of drugs and the insidious influence of liquor.

Proper doses of paraldehyde produce some physiological effects associated with ethyl alcohol. It has been stated, but not authoritatively supported, that paraldehyde was shipped to Russia from another country (not the United States) to serve as a substitute for vodka. We are familiar with the historic accounts of ether sprees indulged in by the Irish and "Piccadilly Willies," and recent medical literature tells of the successful use of oil-ether cocktails prior to dressings of seriously wounded soldiers. So a variety of intoxicants and exhilarating soporifics are actually available, but their names and associations are those of *drugs*, hence their use is not common. If we can but divorce the name and promote the recognition that these "-ol" bodies are in fact drugs and dangerous, liable to produce blindness, the very element of fear alone will have a most salutary effect in protecting men and women from themselves.

Producers of 90 per cent. of the refined methyl hydroxide in this country have decided that hereafter all packages containing it shall be labelled "methanol," and so their advertisements read in the trade journals this day.

This change in nomenclature has been recognized, but the usage cannot be brought about instantaneously and will require time. The word will continue as a synonym in any event, although through concerted action it may become more or less obsolete. No form of legislation can eliminate the name. This is an appeal to chemists to assist.

THE DETERMINATION OF HYDROCYANIC ACID.*

By R. Leitch Morris, F.I.C.

For the determination of cyanides, a number of volumetric processes have been used.

The principal are:

1. The original process of Liebig: Titration of the alkaline cyanide solution with standard silver solution.

This is quite satisfactory when properly carried out.

*Reprinted from *The Pharmaceutical Journal and Pharmacist*, July, 24, 1920.

2. Method of Fordos and Gelis: Little used, but useful in special cases, *e.g.*, for mercuric cyanide.

3. Volhard's method: Complete precipitation as silver cyanide by adding excess of standard silver solution, filtering, and then determining the excess of silver in the filtrate by standard thiocyanate.

4. Titration of cyanide by Mohr's method, using potassium chromate indicator of the complete precipitation.

5. Denigès' modification of Liebig's process, on which the process of the B. P. 1914 is based.

LIEBIG'S ORIGINAL PROCESS.

Properly applied, this method is quite satisfactory, but when free hydrocyanic acid is in question there are several possible sources of error.

The acid must be saturated with but a slight excess of NaOH to form the cyanide, and any *great* excess of NaOH delays the end-point, hence leading to somewhat higher results. But a *deficiency* of NaOH causes a much more serious error, the results being then too low, and the greater the deficiency of NaOH the lower are the results. Results may be obtained showing only a mere fraction of the true strength in such cases: a serious matter in the testing of such a poisonous medicinal agent as hydrocyanic acid.

In the older analytical textbooks the directions are given to make the solution of HCN strongly alkaline, but since NaCN and KCN are strongly alkaline to litmus, this is no safe guide. A strongly alkaline reaction to litmus paper is obtained when only 10 per cent. of the free acid present is saturated. In such cases the process of Liebig gives the end-point when the *NaCN* present is converted completely into AgCN, NaCN, and so determines at this point the NaCN present. If, now, the free HCN remaining in solution is saturated with NaOH, the titration can be continued. The extra silver now used is equivalent to the free hydrocyanic acid remaining unsaturated at the first addition of the soda. When a solution contains alkaline cyanide and also free HCN this last process of titration allows of the determination of both in the same lot of solution.

These points were communicated to the meeting of the B. P. C. in 1874 in an excellent paper by Siebold. He stated that, for every 10 Cc. of normal soda present in excess of that required to form NaCN, an additional 0.1 Cc. of $N/10$ $AgNO_3$ was required. The error is small in this case, and even if this excess has been used, the

error on a 2 per cent. acid would only affect the percentage found, by a unit in the second decimal, if about 20 Cc. of $N/10$ $AgNO_3$ were used. Evidently one is quite safe if the excess of soda is kept at about the equivalent of 1 or 2 Cc. of normal NaOH.

A study of the reactions involved explains the difference between Liebig's and the other processes in above list.

(*a*) When a solution of HCN or of an alkaline cyanide is added slowly to an excess of silver solution, precipitation of AgCN is immediate. The continued addition of HCN only increases the precipitate till all the silver is converted into AgCN. But continued addition of alkaline cyanide causes the precipitate first formed to redissolve as the double cyanide.

(*b*) Reversing the order of mixing: $AgNO_3$ added slowly to an alkaline cyanide gives no permanent precipitate till all the cyanide is changed to the double salt, then the next drop of $AgNO_3$ solution causes the beginning of precipitation of AgCN (the end-point in Liebig's process). The final *complete* precipitation of cyanide as AgCN is accomplished by adding exactly as much silver again as that used to cause the first sign of precipitation.

The equations representing *a* and *b* are:

(*a*) $HCN + AgNO_3 = AgCN + HNO_3$
$KCN + AgNO_3 = KNO_3 + AgCN$ } complete precipitation of both CN and Ag

(*b*) $2KCN + AgNO_3 = \underline{KCN, AgCN} + KNO_3$

No precipitate till this stage (*b*) is complete. End-point of Liebig's process.

The addition of more $AgNO_3$ precipitates AgCN.

Another molecule of $AgNO_3$ gives the same final result as (*a*):

$2KCN + 2AgNO_3 = 2Ag\,CN + 2KNO_3$ } complete precipitation of both Ag and C.
i.e., $KCN + AgNO_3 = AgCN + KNO_3$

A point obvious from these equations which seems to have escaped notice is that since, in Liebig's process.

2HCN or 2KCN is equivalent to $AgNO_3$,
similarly 2KOH or 2NaOH is equivalent to $AgNO_3$.

And therefore, the amount of alkali required for exact conversion of the HCN into cyanide is twice as many Cc. of $N/10$ NaOH (or KOH) as the number of Cc. of silver solution used.

i.e., No. of Cc. of $N/10$ silver required $\times$ 2 = Cc. of $N/10$ soda that should be used to convert the HCN into cyanide.
No. of Cc. of $N/1$ silver $\times$ 2 = Cc. of $N/1$ soda required.

Taking 5 Cc. acid of 2 per cent. strength, which should require not more than 19 Cc. $AgNO_3$, the amount of $N/10$ soda required would be 38 Cc. In this case the use of 4 Cc. of normal soda will ensure accurate results. Also, more than 10 Cc. of $N/1$ soda should never be used, since this is sufficient for a titration in which 50 Cc. of $N/10$ $AgNO_3$ are required.

From equations (*a*) and (*b*) it is obvious that in the case of HCN the addition of alkali is necessary to allow the Liebig reaction to take place by converting finally the NHO_3 which would otherwise be liberated into KNO_3.

Evidently, for this purpose, alkaline carbonates would serve as well as hydroxides, and at first sight it would seem that this is an easy way of overcoming the difficulty by keeping the excess of alkali required sufficiently low. Were HCN not a volatile substance, such would be the case, but since HCN is a very weak acid, which barely reddens litmus, and *does not decompose carbonates*, it is obvious that, at the beginning of the titration, all the HCN present is in the free state, and some free HCN will be present up to the end, and this leads to loss owing to the continual agitation of the solution during titration.

After adding excess of alkaline hydroxide, however, this excess can be considerably reduced by the addition of a little sodium bicarbonate.

$$NaON + NaHCO_3 = Na_2CO_3 + H_2O.$$

Influence of Other Substances on Liebig's Process.—Ammonium salts *would not interfere, but free NH_3 does so*, as AgCN is soluble in ammonia, and if ammonium salts are present some free NH_3 will be liberated by the excess of alkali. This can be overcome by addition of a little carbonic acid water; a bottle or syphon of aerated water is useful for the purpose. Addition of $NaHCO_3$ is not suitable here.

Chlorides, bromides, and iodides do not interfere. Squire states in last two editions of the *Companion* that chlorides are also estimated in Liebig's original process, *but this is an error.*

If halogen salts are present the end-point (precipitation) is shown by the precipitation of the silver *halides*, which are *more* insoluble than AgCN, and this tends to make the end-point *sharper*. The average error in Liebig's process, should not exceed 2–3 parts per thousand too high. In Liebig's process 1 Cc. $N/10$ $AgNO_3$ = 0.005,-404 Gm. HCN.

2. METHOD OF FORDOS AND GELIS.

This is also a very old process. The reaction was discovered by Serullas and Wöhler. $HCN + I_2 = HI + ICN$. Hence I_2 is equivalent to HCN (or KCN) and 1 Cc. of $N/10$ iodine = 0.001351 Gm. HCN. *Starch must not be used* as indicator, as its presence leads to low results. The solution must be highly diluted. In the case of alkaline cyanides, the solution, containing about 0.05 Gm. of cyanide, is diluted to about 400 Cc., a little CO_2 water added, and iodine solution run in till a faintly visible yellow appears in the solution. In the case of HCN, sufficient NaOH is added to convert the acid to cyanide, excess of carbonic acid water added to convert excess of NaOH into bicarbonate, and the solution titrated in the same way. The results are generally a little *lower* than those obtained by Liebig's process, but are fairly close to the truth, although a little excess of iodine is necessary at this high dilution to give the solution the faintest visible tint. The process is somewhat troublesome for hydrocyanic acid. It is a useful process for determining CN in HgCN.

3. VOLHARD'S METHOD.

Volhard's method is only useful in special cases. It is highly accurate, but the necessary filtration of the silver cyanide before the excess of silver can be determined makes the process tedious. All the halogen elements interfere. In this case, 1 Cc. $N/10$ $AgNO_3$ = 0.002702 Gm. HCN.

4. MOHR'S METHOD.

This resembles the usual titration of chlorides, etc., by $AgNO_3$ using K_2CrO_4 as indicator. The solution must be neutral and in the case of HCN this is accomplished by using MgO. The reaction is different from Liebig's reaction, since the end-point shows the complete precipitation of cyanide; equation (*a*) above. 1 Cc. $N/10$ $AgNO_3$ = 0.002702 HCN. The acid is added to excess of MgO which must be chloride free, and titrated with silver as usual, with continual stirring. Though at one time official in U. S. P., the process has no advantage over that of Liebig.

5. MODIFICATION OF LIEBIG'S METHOD. (DENIGÈS)

Denigès (*Journ. de Pharm.*) [5] (XXIX) suggests the use of KI as an indicator in solutions rendered strongly alkaline with soda or ammonia, and states that in this manner the end-point is sharply

and quickly determined. (See *Y. B. P.*, 1894.) This causes at the end-point the precipitation of AgI, which is the *most insoluble* of all silver salts, and thus gives the most accurate results in any modification of Liebig's method. Again, since AgI, unlike AgCl and AgBr, is highly insoluble in ammoniacal water, the substitution of ammonia for the soda required in Liebig's process becomes possible, and a considerable excess of ammonia does not interfere. The use of ammoniacal KI solution has long been employed as indicator in the cyanide titration of nickel. The process of the B. P., 1914, is based on this method. I found it highly accurate ten years ago, but the "Conference Research List" says that it is unsatisfactory, and I have been led to look up the exact details given in the B. P. and to compare them with those I followed, and also with those given by the U. S. P. and the French Codex.

The compilers of the B. P., 1914, have apparently copied from the U. S. P., and have overlooked the fact that the U. S. P. solution of KI is a 20 per cent. one, while the B. P. solution is only 10 per cent., yet the amount to be used is 3 drops in each case. On further comparison of these processes it appears that at the *end* of the titration of the U. S. P. process the total volume of solution will be about 37 Cc., while at the end of the B. P. process the volume will be about 80 Cc. Hence, in the B. P. process the mass concentration of KI in the solution at the end-point is only about a *fourth* as strong as in the U. S. P. process. It would seem, therefore, that the B. P. prescribes too little KI for the process to give a sharp end-point. May not this be the reason that the B. P. process has been found unsatisfactory?

The French Codex orders 10 drops of solution of KI (20 per cent. wt. in wt.) to be used with 10 Gms. of acid and 15 Cc. of NH_3 solution and dilution to 200 Cc. Here the mass concentration of KI in the final volume is practically three times that of the B. P. I used 0.1 to 0.2 Gm. of KI in working on this process.

Another suggestion to improve Liebigs' process is due to Guerin in 1906, who recommended the use of a 3 per cent. solution of borax as the alkaline agent in place of NaOH. This is excellent. I found the amount of silver used in comparative titrations agreed exactly with that required by the original Liebig method when the excess of alkali was kept as low as possible in the latter method. Any excess of borax is immaterial. Guerin states that ammonium salts must be absent, but that this difficulty can be avoided by adding 10 Cc. of

saturated solution of boric acid to the liquid before titration. I have not verified this last statement.

EXPERIMENTAL.

The results given were obtained in 1909. This work was an extension of some work on cyanide solutions, in which the ammoniacal iodide process had given the best results as compared with other methods.

As a standard for comparison the HCN was determined gravimetrically by weighing as silver cyanide, and, as a check, igniting the silver cyanide to constant weight, and weighing again the residual metallic silver. To prevent loss by volatilization the acid was added to sufficient ammonia in a stoppered flask, after previously ascertaining the weight of flask + NH_3 solution and the total weight again found. The mixture was transferred to a beaker, excess of silver nitrate solution added, and then the whole acidified slightly with dilute HNO_3.

The precipitate was collected on asbestos in a Gooch crucible, dried at 100°–105° C. to constant weight. To convert the AgCN to silver, the Gooch crucible was transferred to an ordinary crucible of the same shape in which it just fitted, and ignited fairly strongly to constant weight. In the volumetric work (Series A) from 50–60 Gms. of the acid were weighed out similarly into a flask containing the NaOH or NH_3, respectively, and the whole diluted in a measuring flask to a definite volume, aliquot portions being drawn off for the titration.

The mean results by the gravimetric process may be taken as very close to the true strength by weight of HCN.

In Series A, below, the individual determinations were made on the same day as the gravimetric process, since the solution, even after mixing with the alkali, is not of constant strength.

The results may be regarded as fairly comparative. The amount of $N/10$ silver solution varied from 40 to 46 Cc., so that the errors of reading are negligible in final results.

Measuring flasks, burettes, etc., were standard (verified at Charlottenburg).

The hydrocyanic acid used was prepared in the laboratory (from pure materials, by distilling K_4FeCy_6 with dilute sulphuric) in order to ensure absence of HCl (a trace of which is said to be added to the commercial acid).

Presence of any free HCl would raise the apparent amount of HCN in the gravimetric and Volhard processes. The acid was diluted to contain rather less than 2 per cent. HCN.

All calculations and strengths of standard solutions were based on the International Atomic Weights, 1909; for silver, nitrogen and carbon the atomic weights are the same at the present day.

SERIES A.

Process.	(Results by weight in weight.)
Gravimetric (as AgCN)	(*a*) 1.650%; (*b*) 1.643% } mean of 4 = 1.647%
Gravimetric (as Silver)	1.648%; 1.645 } (gravimetric).
Volhard (1 determination only)	1.651%. .
Original Liebig (excess of NaOH slight)	mean of 6 = 1.650%
Fordos and Gelis	mean of 6 = 1.645%
Using NH_3+KI	mean of 6 = 1.648%

SERIES B.

(Same stock of acid, but two months later.)
Acid measured off by pipette (20 Cc.)

Original Liebig process.	Mean of 4 = 1.216 w/v.
Using borax	Mean of 4 = 1.215 w/v.
Using NH_3+KI.	Mean of 4 = 1.213 w/v.

(All results obtained on the same day.)

The iodide method adopted was to use about equal volumes of 10 per cent. ammonia solution and dilute hydrocyanic acid, adding from 0.1 to 0.2 Gm. of KI. The results certainly seem to show that the end-point is sharper with this modification, especially when over 40 Cc. (as in Series B) of $N/10$ $AgNO_3$ was required. In this case using the same amount of HCN the amount of $N/10$ $AgNO_3$ required was 0.03 to 0.05 Cc. less than that required by Liebig's process.

ACTION OF GLYCERIN AS A PRESERVATIVE.

Williams (*Y. B. P.*, 1874–1878) recommended the addition of glycerin for this purpose—20 per cent. was found to preserve the B. P. acid almost indefinitely. Some of the 1.65 per cent. acid of Series A was mixed with sufficient glycerin to make the mixture contain 25 per cent. glycerin. This was found to contain 1.23 per cent. HCN w/v. when made up. Nine months later it still contained 1.19 per cent.

The acid remaining after Series B analyses were finished was allowed to stand for the same period in diffused light. The strength was then 0.15%.

SUMMARY.

It has been shown that Liebig's process for HCN properly conducted gives quite satisfactory results, but that Guerin's suggestion of using borax solution avoids the uncertainty that may occur through the use of too much alkali. Comparison of the B. P. process with that of the U. S. P. and the Codex shows that the B. P. apparently prescribes too little KI. However, if three or four times more KI is used the process agrees well with the gravimetric results. It seems probable that any defect in the B. P. process may be due to an insufficiency of iodide.

YEAST ENZYMES.*

All brewers are aware that considerable differences in attenuative power are exhibited by various brewery yeasts, but it is not so well known that this is in great measure due to the nature and quantity of the enzymes they secrete. According to our contemporary the (London) *Brewers' Gazette*, investigations by many scientific, observers have proved the truth of this and one has to recognize the remarkable fact that ordinary brewers' yeast used very day is able to secrete a number of enzymes, and each of these have a specific function to perform in carrying out the complex reactions associated with fermentation. When the nature of these reactions is fully understood the relationship which exists between attenuative power and enzyme action becomes more apparent. The first enzyme to be discovered in yeast was invertase. This type of enzyme has the power of inverting cane sugar, and that present in ordinary worts is quickly converted into a mixture of dextrose and levulose before actual fermentation commences. So readily does this yeast enzyme act that a well-known process for making invert sugar in the brewery is based upon the action of this enzyme. The optimum temperature for effecting this process is about 130 degrees F.; but lower temperatures, such as those within the range of ordinary fermentation, are sufficient to enable this enzyme to exercise its action upon any cane sugar, generally present in small amount, which may find its way into the fermenting vessel. This inversion of cane sugar into equal proportions of dextrose and levulose must take place, before actual fermentation, caused by the enzyme zymase, can take place. It is nearly thirty years ago since J. O'Sullivan demonstrated that

* From *Pure Products*, October, 1920.

this inversion takes place, under normal conditions, within the cell, since it was found that invertase cannot pass out of the yeast cell by exosmosis.

In a similar manner, maltose which is also a di-saccharide, like cane sugar, must also be reduced to a simpler form by the active agency of another enzyme before fermentation can take place. To this enzyme, the name maltose has been given, and while its presence was suggested by Bourguelot as long ago as 1866, its actual existence in yeast was only demonstrated by Emil Fischer and others in more recent years. Under normal circumstances, the decomposition of the di-saccharide maltose into the monosaccharide dextrose takes place within the yeast cell. As the result of these investigations it has been proved that neither a biose, triose or a polysaccharide is directly fermentable. All have to be reduced to the simpler monosaccharide or hexose form. At one time it was believed that certain moulds, *Monila Candidad*, for example, was able to ferment cane sugar without preliminary inversion, but later investigation showed that this organism contained an invertase which affected the hydrolysis of cane sugar in a similar manner to that of the yeast cell. In addition to the two sugars, cane sugar and maltose, brewers' wort also contains a number of complex carbohydrates, such as dextrin and intermediate bodies, known generally as malto-dextrins. These, as every brewer knows, have an important bearing upon the character and stability of beer, and have much to do with the condition and life which characterizes a well-brewed beer. It is quite obvious that some degradation of these substances takes place in cask, and fermentation proceeds, after the normal or primary fermentation has been completed, and this is due to the fact that certain yeast secrete diastase, and are, therefore, capable of hydrolyzing the complex carbohydrates slowly, and so enabling a gradual but steady fermentation to takes place. Yeasts, and even the ordinary mixed yeasts of the brewery, differ in their capacity for cask fermentation, hence, in a perfect yeast, if one excludes the use of foreign yeasts, which do not readily accommodate themselves to a wort of beer, one requires the power of degrading certain complex carbohydrates, such as the so-called malto-dextrins. It is in this respect that the various types of yeast differ so much in respect to attenuative capacity. That *Saccharomyces Cerevisiae* is admirably suited to the fermentation of the brewers' worts is plain from a consideration of the enzymes enumerated. The cell contains

these entities for the degradation for nearly every carbohydrate found in ordinary worts. Its suitability for general purposes is more apparent when the characteristics of other saccharomyces are considered. For example, one well-known yeast, *Sacch. Apiculatus*, the pear-shaped cider yeast, possesses no hydrolyzing enzyme, and is, therefore, quite unable to ferment disaccharides, such as cane sugar, molasses, etc. Another yeast, *Sacch. Albicius*, is able to hydrolyze and then ferment maltose, but contains no invertase, so that the cane sugar remains unchanged. On the other hand, *Sacch. Kephir*, the yeast employed in the fermentation of milk-yielding Koumiss, can ferment both sugar cane and lactose, but since it does not contain maltose, maltose is unaffected by its presence.

AN HISTORICAL REVIEW OF THE PREPARATION OF QUININE SULPHATE IN JAVA AND IN BRITISH INDIA.*

We are indebted to Herr P. Van Leersum, the former director of the Japanese Government cinchona plantation, whose decease we announced last week, for a valuable and interesting contribution on the development of the quinine industry in British India and in Java ("Algem. Landbouwweekbl. v. Nederl. Ind.," No. 46, 1920). In his introductory remarks he states that the Indians are credited with having discovered the value of cinchona bark, whereas von Humboldt ascribes its introduction to Europeans, who casually discovered the bitter taste of the bark, and, in common with other bitter remedies, employed it in the treatment of fever. The Spanish doctor Villerobel was probably the first to bring some of the bark to Spain in 1632, and there it was first tested in 1639 by a priest in Alcada. Another tradition records that Don Jaun Lopez de Vega, medical attendant to Count Del Chinchon, Viceroy of Peru, received a quantity of cinchona bark from Don Jaun Lopez de Carnizares, Corrigedor of the province of Loja, and with it cured, in 1638, the wife of the Viceroy. On her return to Spain in 1640 she brought some of the bark with her, and thus laid the foundation of its use; in fact, for a long time it was known as *Pulvis comitissae*. The original home of the different varieties of cinchona is to be found in Boliva, Peru, Ecuador, Colombia, and Venezuela. The ruthless manner in which the bark was obtained led to the wholesale destruc-

* From *The Chemist and Druggist*, August 28, 1920.

tion of the trees, and during the first half of the past century many travellers discussed the possibility of cultivating cinchona in other parts of the world. The first plantation of this valuable tree was undertaken by Markham in 1859 in British India, while the planting of seventy-five cinchona plants at Tjibodas in 1854 marked the beginning of its cultivation in Java. Prior to the isolation of its alkaloids, cinchona was used in the form of powdered bark, decoctions, extracts, etc. The following are the principal cinchona alkaloids:

Quinine, discovered by Pelletier and Caventou in 1820.

Quinidine, discovered by Henry and Delondre in 1833.

Cinchonine, discovered by Duncan in 1820, and made known by Pelletier and Caventou.

Cinchonidine, discovered by Winkler in 1848.

In addition there are numerous other substances present, such as quinamin, conchinamin, pariein, etc.

In view of the fact that about 95 per cent. of the bark is of no use to the manufacturer of quinine, it is evident that already at an early date in the history of quinine production steps were taken to obviate the necessity of conveying the whole bark a long distance to a factory—for instance, to Europe. Already in 1793 mention is made of an extract of cinchona prepared in South America, and in 1820 an extract of cinchona was imported into Hamburg bearing a label with "Extracto superior de Quina de la Fabrica de Benito Sebastian & Co., Cuzco." In 1841 there existed a quinine factory in Bolivia, but since the product was very impure it was little in request. Delondre, who was himself a manufacturer of quinine, erected in 1847 a factory in Valparaiso, which was closed in the following year. The first production of quinine in Asia took place at Ootacamund, in British India, and the author refers very fully to Broughton's enterprise in this connection. The method adopted by the latter fifty years ago is not without interest. Briefly, it consisted in boiling the fresh bark with 1 per cent. sulphuric acid; the liquid was then evaporated to one-sixth of its volume, transferred to a wooden vat and an excess of lime water added; after filtering, the precipitate was dried, mixed with alcohol, to which a little sulphuric acid was added, and by precipitation with caustic soda a product was obtained which Broughton called "amorphous quinine." This was stated to contain 18 per cent. of quinine, 54 per cent. of cinchonidine, 13 per cent. of cinchonine; amorphous

alkaloid and coloring matter together, 15 per cent. At that time the cost of production for one ounce amounted to one rupee, and it was sold by the Indian Government at the rate of 1 rupee 8 annas.

In 1873 C. H. Wood was intrusted by the British Government with the task of investigating the possibilities of preparing quinine from the Bengal plantations, particularly in Skikkim. He followed practically the same method as adopted by de Vrij, which yielded an amorphous white powder, known in India as "Cinchona Febrifuge" (in Java it was termed by de Vrij "Quinetum"), which in 1875 was sold by the Indian Government at 20 rupees a pound. The first attempts to manufacture alkaloids from the bark in Java were made in 1870, further investigations were undertaken in 1872 by Moens, and in 1877 Eydman introduced de Vrij's process. This consisted of extracting the bark with 1 per cent. hydrochloric acid for three days, and then precipitating the alkaloids by caustic soda. The residue was dissolved in dilute sulphuric acid and a precipitate obtained by the addition of caustic soda.

In 1900 Van Leersum secured the assistance of an expert staff at the Bandoeng factory, of which he was appointed director in 1902, and immediately set to work to sove the problem of the manufacture of pure quinine in Java. He then discussed the various factors which have to be considered in the manufacture of a pure product, and the difficulties that have to be overcome, which may be briefly referred to in the following points.

Calcium hydroxide is the best base for separating the alkaloids from the bark, but in order to render the cell walls permeable to the calcium hydroxide, the addition of sodium hydroxide is necessary, and powdered bark, calcium hydroxide, and sodium hydroxide must be intimately mixed. The relative proportions are 30 parts of fine slacked lime to 100 parts of finely powdered dry bark, and 90 parts of a 0.5 per cent. solution of sodium hydroxide for each 100 parts of bark. This mixture is placed in an extractor, and, under the circumstances, the best extractive is benzol with a high boiling point or toluol of 120 degrees C. boiling-point, which dissolves quinine 1 : 3. Petroleum and other earth oils have also been used as extractives; if the latter are employed the alkaloids are extracted by the addition of dilute sulphuric acid. If a substance is used which can be distilled off, *i. e.*, benzol, dilute acid is first added to retain the alkaloids in solution when removing the solvent by distillation. The acid solution of alkaloid is brought to boiling by steam, neutralized by the

addition of solution of caustic soda, and the solution of quinine is poured into crystallizing pans. The crude product is dissolved in dilute sulphuric acid, heated to boiling by steam, neutralized, and then filtered through charcoal. After crystallizing the crystals are centrifuged, washed and dried. The latter process has to take place in the dark, and red or yellow glass must be used for the windows of the room in which this is done, since quinine sulphate loses its white color on exposure to light. He mentioned that the appearance of the salt influences the price it commands—thus Howard's quinine is the highest quoted on the market owing to its fine appearance. The more voluminous it is the higher its value. Pure quinine sulphate does not yield such fine crystals as a product containing a certain amount of cinchonidine. Since the various pharmacopoeias permit the presence of a certain amount of cinchonidine in quinine, this is taken into consideration, and as Ledgeriana contains very little cinchonidine, Succirubra bark is mixed with the latter; Succirubra contains from 1 to 3 per cent. of cinchonidine.

The author then referred in detail to the manufacture of quinine from fresh bark by a process found after numerous experiments. Twenty-five grams of fresh bark are cut into small pieces and 2.5 grams of slaked lime are added. After pounding from five to ten minutes in a mortar the mass is sufficiently fine to be extracted. It is important to add exactly ten per cent. of slaked lime. It is best extracted with toluol of a boiling point of 120 degrees C., and then submitted to the process described above. Van Leersum, in conclusion, strongly advocated extensive trials to establish the advantages of manufacturing quinine from fresh bark, as this process would reduce the cost of production of this precious drug. He favored the creation of a government experimental laboratory, and referred to attempts made by quinine manufacturers to purchase the rights of this process, which is being found satisfactory, although worked on a modest scale with imperfect machinery, in the factory of K. A. R. Bosscha in Malabar. He reckons that the cost of producing one kilogram of quinine sulphate by this new process and making therefrom 5,000 tablets would amount to three florins, whereas the present cost of production amounts to 6.5 florins. It takes on an average 18 kilograms of dry bark to produce 1 kilogram of quinine sulphate, the average cost of 1 kilogram of bark being about 32 cents.

AN IMPROVED METHOD FOR THE ASSAY OF ACONITE PREPARATIONS.*

By E. J. Chappel, A.I.C., and Noel L. Allport.

The standardization of tincture and liniment of aconite was made official for the first time in the 1914 edition of the British Pharmacopoeia. In the method to be adopted for their assay the analyst is left to base his process upon that described for the root. According to this method, the liquid preparation is evaporated to dryness at a temperature not exceeding 60°, and the solid residue is then dissolved in $N/50$ sulphuric acid. The resulting solution is next filtered but this operation is often so slow and tedious that a more expeditious method is needed. It is claimed that this disadvantage is overcome in the modified process here described.

It has been proposed by others to extract the acid liquid with ether, without previous filtration, but this gives troublesome emulsions, and we have found the use of petroleum ether to be much better, as there is no such tendency with this solvent. Other solvents were tried, but none was found to give such easy manipulation as petroleum ether. As the result of many experiments the following method is recommended:

15 Cc. of the liniment or 100 Cc. of the tincture are evaporated at a low temperature to remove the bulk of the alcohol. 5 Cc. of 10 per cent. sulphuric acid diluted with 20 Cc. of water are added, and the whole transferred to a separating funnel, with the assistance of a glass rod to break up the separated resin; the dish is then rinsed carefully with a little water.

About 20 Cc. of petroleum ether (B. P. 40°–60°) are added, and the mixture shaken. Separation is rapid, the aqueous liquor is drawn off and again shaken with petroleum ether. The two petroleum liquors are mixed, rinsed twice with water, and the washings added to the acid liquid, which is then rendered alkaline with ammonia and extracted four times with either. The ethereal extracts are washed successively with the same portion of water, after which they are run into a flask and evaporated to dryness. The alkaloidal residue is dried at a low temperature to ensure removal of ammonia, and then titrated in the usual manner.

The great advantage is the saving of time in avoiding troublesome filtration, which may take several hours. The process may be

*Reprinted from *The Pharmaceutical Journal and Pharmacist*, July 24, 1920.

equally applied to the assay of the root by first preparing a tincture as directed in the Pharmacopoeia.

The results obtained by this modified method are to all intents and purposes identical with those given by the more lengthy process of the British Pharmacopoeia. as the following table shows:

ETHER SOLUBLE ALKALOIDS.

	B.P. Process.	Modified Process.
Tincture	0.039 per cent.	0.035 per cent.
Liniment	0.199 "	0.206 "
"	0.193 "	0.196 "
"	0.193 "	0.196 "
"	0.209 "	0.212 "
"	0.257 "	0.254 "
"	0.196 "	0.193 "

These experiments have been carried out in the laboratories of The British Drug Houses, Ltd., to whom we are indebted for permission to publish the results.

THE CAMPHOR INDUSTRY IN FOOCHOW.*

BY VICE CONSUL ERNEST B. PRICE,
FOOCHOW, CHINA, JUNE 23, 1920.

Stocks of camphor now in the hands of local Foochow dealers are estimated at 80,000 pounds and of camphor oil at 40,000 pounds, while in the hands of the Government Camphor Bureau there are about 27,000 pounds.

The current market price in Foochow for camphor is 98 taels ($98 at prevailing exchange rate) for 133 pounds, and for oil 40 taels ($40) per 133 pounds. These prices are unusually low. About a year ago camphor was quoted at 200 to 220 taels. (At that time the tael was worth nearly $1.50 United States currency, so that the price of camphor was between $300 and $330 per 133 pounds.) The causes of the present low prices seem to be three—governmental restrictions on production and distillation, lack of demand from Hongkong, and a general slackening of business owing to difficulties of production and transportation.

There has been, however, a surprising amount of export, considering what conditions are. During the calendar year 1918, 56,533 pounds, valued at $33,536, were exported from Foochow; in 1919,

* *Commerce Reports*, Aug. 18, 1920.

931,600 pounds, valued at $642,929, were exported; during the March quarter of 1920, 427,066 pounds, valued at $268,413, were exported, representing a considerable increase.

Methods of Distillation and Transportation.—Trees fit to be used for camphor distillation must be at least 20 years old. When a suitable tree is found a crude native distillery is set up at the spot. This consists of a boiler, with an iron base and a wooden top, connected to a distilling vat partially filled with water. The camphor upon being conducted to the vat precipitates as crystals on the inner walls, while the nonprecipitable portions drop down as oil, which floats upon the water. About $5^1/_4$ pounds of camphor and camphor oil, in the proportions of 70 per cent. camphor and 30 per cent. camphor oil, can be produced from 240 pounds of chips.

The districts where most of this initial distillation is done are Kienning, Yuchi, Yungan, Yenping, Tatien, Shaowu, Shahsien, and Ningte.

It is almost impossible to say how many men are engaged in the industry, but there cannot be many. Their wages are equal at the present rate of exchange to about $0.38 a day.

The crude product is carried by porters to the Min River, or one of its tributaries, and then carried to Foochow by native boat. Boat hire is approximately $1 per hundred pounds from the interior to Foochow.

How Marketing Is Done.—The marketing of camphor is done very largely through brokers in Hongkong. The distillers seldom do their own marketing, with the exception of the Japanese and Portuguese. There are also brokers in Foochow able to handle foreign orders in the English language.

It should be borne in mind that the camphor market is an extremely sensitive and dangerous one for the uninitiated. The factors of supply, governmental supervision, freights, stocks in Foochow and Hongkong, and three markets—Foochow, Hongkong, and the foreign market—all enter into the situation. Hence, no better scheme than the brokerage system can be suggested, unless the foreign buyer is prepared either to go into the producing end of it or into the buying and holding of considerable stocks himself.

The product as it leaves the distillery in the interior consists of crystals and camphor oil. The crystals are ready for marketing, but the oil is put through a process of redistillation at Foochow. This process is a simple one, and need not be described here in de-

tail. The effect is to distil from the oil all the remaining camphor; 133 pounds of oil produce 64 pounds of camphor and 27 pounds of desolated oil. The camphor derived from oil is of a cheaper grade than that derived originally from the wood chips. The desolated oil is used as a base for dyes and paints.

There are 12 of these distilleries in Foochow which produce camphor from the oil. They are known as the Yuan Cheng, Hsing Chi, Cheng Chi, Hsiang Chi, Fu Sheng, Hsieh Chi, Kao Fang, and Tao Ho—all Chinese; Ting Te—Portuguese; and Mitsui Bussan Kaisha and Tai Hua—Japanese. When working, each distillery produces on an average of 325 pounds of camphor a day.

The Government Camphor Bureau.—The various districts producing camphor have each an official camphor bureau under the control of the Provincial Commissioner of Industry. Each bureau has the authority to collect within the district it covers certain taxes and to buy camphor trees and distil camphor. In American currency the tax is approximately $6 on every 133 pounds of camphor in transit. The taxes collected and the camphor produced are sent to another Government bureau called the Fukien Government Camphor Industry, Transportation, and Tax Collection Office. Its duties are to take in and turn over to the provincial government the taxes remitted by the various district bureaus and to take in and market the camphor received.

There is still a third bureau which has authority to buy camphor oil and distil it into camphor, marketing its product independently.

Private producers must take out licenses and agree to pay the taxes herein-before mentioned. There is also a license fee of $2 local currency per month per vat.

Foreigners wishing to go or send into the interior to purchase camphor under what is known as the "transit pass" system, permitted by treaty, may still do so. Under this system the foreign exporter may bring the native product to the seaboard and export it to a foreign country by paying the regular 5 per cent. export duty plus a surtax of half the export duty. The foreigner may purchase either from the private producers or from the Government bureau. The effect of the Government bureau system is to tax the product just the same, because the foreigner may not operate his own distillery in the interior, and Government taxes are imposed on the distillery and its product before the foreigner purchases the camphor.

Japanese distillers operating in the city of Foochow are not

taxed, according to information given by the Japanese consulate in Foochow.

The Government bureau which markets the Government camphor announces that it sells at Hongkong market rates.

At present camphor is cheap and there are fairly large stocks on hand, but not much is coming in from the interior. Local firms are ready and anxious to do business with Americans.

FURTHER REPORTS ON BENZYL BENZOATE.*

Since benzyl benzoate was introduced into medicine little over a year ago, it has come into very general use in the treatment of diseases in which there is spasm of unstriped muscle.

T. E. McMurray (*N. Y. Med. Jour.*, July 24, 1920, p. 122) reports on its use in whooping cough, in which he obtained satisfactory and immediate results. The dose given was from 5 to 30 minims every four hours, depending on results. In some cases the smaller dose was sufficient, and in almost every case the paroxysms subsided. The effect was ususally felt within 48 hours, and in one instance there was relief after the second dose. As a rule the relief is immediate and complete, and the treatment seems to lengthen the interval between attacks. No undesirable results were experienced; in one case a child of 12 months received 20 minims without showing any evidence of gastric or other disturbance.

D. I. Macht (*Johns Hopkins Hosp. Bull.*, July 1920, p. 236) found it acted as a valuable palliative, though not exactly curative, in a large number of cases of whooping cough that had resisted other treatment. He used a 20 per cent. alcoholic solution, giving from 5 to 40 drops in water three or four times a day or oftener, according to the age of the patient, and the severity of the disease. A few drops of benzaldehyde (essential oil of bitter almonds *sine* HCN) added to the solution not only makes the dose more palatable to children, but seems to increase the palliative effect.

D. I. Macht (*Med. Record*, July 24, 1920, p. 146) has found the drug most valuable in hiccough, not only in the mild form so common in infants, but in the more persistent forms which last for long periods of time. He cites several cases of persistent hiccough in adults in which relief was obtained with one or at most a few doses. Macht thinks that benzyl benzoate may also be of diagnostic value

* From *The Prescriber*, October, 1920.

in differentiating between hiccoughs of purely central origin and those which are due to some peripheral cause. Inasmuch as the drug acts peripherally on the smooth muscle structures, he thinks that benzyl benzoate will prove most useful in hiccoughs of peripheral origin. He finds the drug acts best when administered in 20 per cent. alcoholic solution, in doses of from 20 to 40 drops in water or milk. Suspensions or emulsions are not satisfactory, and capsules have been found to cause local irritation, or to render the action too slow.

A. D. Hirschfelder (*Minnesota Med.*, Aug., 1920, p. 380) says that benzyl benzoate gives relief in many (though by no means all) cases of bronchial asthma. He has used it in other conditions of spasm, and has had striking results in the treatment of *dysmenorrhoea*.

E. A. Heller and E. Steinfield (*New York Med. Jour.*, July 31, 1920, p. 160) report on the *non-leucotoxic properties* of benzyl benzoate. Because of its close chemical derivation from benzol (benzene, B. P.), it appeared to them to be desirable to investigate any possible analogy to the toxic effects of the latter. Experiments were accordingly made on rabbits; several preliminary leucocyte counts were made in order to note any tendency to variation, and the animals were then given subcutaneous injections of a mixture of benzyl benzoate and olive oil, in equal parts. The dose varied from 1 Cc. to 2.5 Cc. per kilo of body-weight. Two animals were used as controls to demonstrate the destructive effects of benzol. Leucocyte counts were made daily until a tendency to consistency was noted and then every other day. The animals receiving benzyl benzoate showed no appreciable difference in leucocyte count, though those receiving the largest doses exhibited lethargy, weakness, and in one case death. In contrast, the two control animals receiving benzol showed definite evidences of depression of the leucocyte count, which later came back to approximately normal. The authors conclude that, unlike benzol, benzyl benzoate is without toxic effects upon the leucocytes and that there is a wide margin of safety between its therapeutic and its toxic doses.

D. I. Macht (*N. Y. Med Jour.*, Aug. 28, 1920, p. 269) reports on its use in some circulatory conditions. He finds the drug to possess powerful vasodilator properties, without being depressant to the heart when administered by the mouth in small doses. Owing to this property it has been found effective in the treatment of

hypertension and angina pectoris. The best method of administering the drug in such cases is in alcoholic solution which admits of rapid absorption and a control of the dose.

THE EFFECTS OF AIR POLLUTION BY SMOKE AND ITS PREVENTION.*

By J. B. Cohen.

The Smoke-Abatement Committee, appointed by the Minister of Health, after taking a large amount of expert evidence, has issued an interim report on what may be termed "domestic smoke." The object of this report is mainly to furnish information as to the best methods of preventing smoke in connection with the new housing schemes to which the Ministry is offering large subsidies, and which consequently have to receive its approval. Incidentally, the destructive effects of coal smoke and the wastage of fuel, as well as the efficiency or otherwise of domestic heating appliances, have been considered. The annual loss of fuel in the form of soot is estimated at nearly two and a half million tons. At the same time, it is pointed out that the presence of soot is an indication that a far more formidable loss is being incurred by the inefficient utilization of the heat from the fuel. Moreover, domestic soot, by reason of its higher content of tar, which causes it to adhere to the objects upon which it falls, is far more destructive and dirt-producing than factory soot, which is a product of more complete combustion and contains less tar and more ash. The following analyses will make this clear:[1]

Constituents.	Original Coal.	Ordinary Grate Flue.	Top of Boiler Chimney —110 Feet.
Carbon	60.30	40.50	27.00
Hydrogen	4.89	4.37	1.68
Tar	1.64	25.91	1.14
Ash	8.48	18.16	61.80

As regards the effect of a smoky atmosphere on health, statistics show that a town fog immediately increases the death rate from respiratory diseases, and the cause underlying this high mortality,

* From *Jour. Soc. Chem. Ind.*, Aug. 31, 1920.—Vide Interim Report of the Smoke-Abatement Committee of the Ministry of Health, 1920. H. M. Stationery Office.

[1] "Smoke, a Study of Town Air," by J. B. Cohen and A. G. Ruston. E. Arnold, London, 1912.

which invariably follows in the wake of a thick fog, must operate, though to a lesser degree, on the general health of the community in an industrial center under normal conditions. More definite evidence was forthcoming of the effects of smoke on vegetation. By shutting out sunlight, by covering the leaf and blocking the stomata with tar, life especially that of evergreen plants and trees is seriously affected. Moreover, the sulphuric acid which is invariably associated with soot, destroys the nitrifying organisms and removes lime from the soil as sulphate. This result has been observed at the experimental farm at Garforth attached to the University of Leeds, where the difference between limed and unlimed soils has exhibited in a remarkable way the action of acid soot. Another indirect result has been the diminished value of grazing land in smoke-infected areas, in consequence of which the rental of these pastures has steadily decreased from year to year.

Equally striking evidence was submitted to the Committee by Sir Frank Baines, Director of H. M. Office of Works, as to the serious damage occasioned to public and other buildings by smoke and other impurities in the atmosphere and especially by the deposit of acid soot. The effect in most cases was due to the removal of the calcium carbonate (which acts as a cement for grains of siliceous material) in the stone becoming dissolved as calcium sulphate and thus causing the siliceous particles to crumble away. In the opinion of Sir F. Baines, the cost of repairs and upkeep of public buildings and monuments (a very heavy expense) would be diminished by one-half if the smoke and the accompanying acid could be eliminated.

This acid soot not only clings to vegetation and to stone, but corrodes brick and metal work, attacks fabrics, leather binding of books, and discolors paint. The Manchester Air Pollution Advisory Board find, in Manchester, in the cost of washing materials alone apart from the labor involved, that more than £250,000 would be saved annually by the absence of smoke. A very careful and exhaustive inquiry by an expert committee of engineers, architects, and sciences estimated that in 1912, in Pittsburgh, U. S. A., the cost due to smoke was £4 per head of the population. If we take as a rough estimate the 20 towns of the United Kingdom of over 200,000 inhabitants having a total population of over 12 millions at 10s. a head, we get a sum of six millions, while the waste occurring accruing from the non-utilization of the by-products from raw coal, such as tar oils, sulphur, ammonia, and cyanogen compounds, so

essential to our chemical industries and motor traffic, must amount to many millions more.

A considerable amount of expert evidence was placed before this Committee on the efficiency of kitchen ranges, and on that of coke and coal burnt in an open fire by Prof. Barker of University College, London,[1] and Mrs. Fishenden,[2] of the Manchester College of Technology. There was a consensus of opinion that the old form of open kitchen range with back boiler was inefficient, wasteful in fuel and labor and productive of smoke.

For cooking, warming rooms, and providing a hot-water supply, the following recommendations were made by the Committee, and, in considering these they were guided by the utility, economy and efficiency of the proposals as regards smoke prevention. They do not recommend any one method, but make the following suggestions: That gas cookers and gas fires are thoroughly hygienic when properly installed; that where an adequate supply of gas is available, a gas-cooker should be substituted for the ordinary coal range; that for intermittent use both gas cookers and gas fires are often more economical than coal fires. That from a hygienic and labor-saving point of view electric cooking and heating have much to recommend them, but the present high price of electricity precludes their general adoption. The cheapest and most efficient method of producing a supply of hot water is a coke-fired boiler. A gas boiler, though more expensive, is very convenient in hot weather. The warming of rooms may be effected by hot-water radiators or gas fires, both of which are quite hygienic if the rooms are adequately ventilated. In this way coal may be dispensed with, and this system has been successfully established at the Austin Motor Company's village at Northfield, near Birmingham, where the warming of rooms by radiators and the hot-water supply were provided for by a coke stove and the cooking was done by gas. No coal entered the village and no smoke issued from it. The foliage and grass retained their fresh and clean appearance, and there was no discoloration of clothes and fabrics from the fall of soot. There is, however, a difficulty in dispensing with an open fire. Custom and sentiment are not easily eradicated, and there is no doubt that the appearance of warmth

[1] Vide Report of the Fuel Research Board for 1918–1919. Appendix B and p. 26.

[2] Coal Fires. By Dr. Fishenden, Air Pollution Advisory Board, Manchester City Council.

is even more important to the comfort of many people than its mere sensation. But this difficulty is in a fair way of being overcome. The production of what is known as low-temperature coke, or semi-coke, or "coalite," which ignites easily and glows with little or no smoke, is being investigated by the Fuel Research Board under the Department of Scientific and Industrial Research, and when this fuel is on the market at a moderate cost, and in sufficient quantity, the domestic smoke problem will be near solution. Meantime a coke stove which can be readily lighted is being perfected by a Halifax firm and has the advantage of being used as an open stove for warmth or closed for heating radiators or the boiler, or both, and for consuming kitchen refuse.

Hence efficiency, economy, cleanliness, and comfort can be obtained to-day if we choose without resorting to raw coal, thus producing an enormous national saving, with the added blessings of pure air, clear skies, and clean foliage.

SIMPLE TESTS FOR ADULTERATION OF TURPENTINE.

Specialists of the Bureau of Chemistry, United States Department of Agriculture, have worked out simple tests for detecting the adulteration of turpentine, as follows:

Since the individual purchaser rarely has occasion and the producer is seldom in a position to make any extensive tests to determine whether a turpentine meets the specifications, it may be stated that the producer, knowing the purity of his product, need examine only to determine whether the turpentine is "standard" in color and whether it meets the specifications for specific gravity and distillation. Should the specific gravity at 15.5°/15.5° C., when carefully taken with an accurate hydrometer or spindle, be between 0.862 and 0.870 (32.4° to 30.9° Bé.), as is the case with nearly all American gum spirits of turpentine, it may safely be concluded that the sample will meet the requirements as to distillation. Should the specific gravity be found very close to the limits of the specifications adopted by the United States Government (0.862 to 0.875 at 15.5° C.), the sample should be examined by a competent chemist qualified to test turpentine. In the case of fresh turpentine which has not been scorched in making, become oxidized by standing in a tank, or been contaminated with oxidized turpentine, no testing is needed. Such turpentine will always pass the specified requirements.

When turpentine is adulterated to the extent of 10 per cent. or more, a careful observer familiar with turpentine can usually determine the fact by one or more of the following simple tests:

Odor.—The presence of kerosene, gasoline, benzol, or solvent naphtha is usually revealed by its odor. Wood turpentine is best distinguished from gum spirits by its odor. The odors of these materials cannot be described; they can be learned only by actual trial and experience. Lack of the characteristic turpentine odor is good ground for a careful test to determine the purity of the sample.

Grease Spot.—Pour a little of the suspected turpentine on a piece of white writing paper. If the bulk of the sample evaporates rapidly from the paper, leaving a greasy spot which evaporates very slowly or not at all, the turpentine is probably adulterated with kerosene or heavy solvent naphtha, or contains a large percentage of heavy turpentine which will not distil below 170° C. The odor of the grease spot often determines the nature of the adulterant. Greasy spots around bung or spigot holes of turpentine barrels are also indicative of these adulterants.

Bead.—When a perfectly clean dry bottle is partly filled with turpentine and violently shaken for a moment the head or foam that forms will immediately pass away if the turpentine is pure and fresh. If the foam persists for 5 seconds or more, the turpentine probably is adulterated or old.

Evaporation Test.—Set a 5-inch watch glass near an open window where a gentle air current can blow across it. Carefully place in it 5 cc. of the turpentine, so that the glass does not become wet with the turpentine beyond the edge of the surface of the liquid. Then carefully pipette or dip out 2 Cc., or about half of it. Observe the rim of the turpentine film after 3 hours. If the rim is continuous or more or less regular in outline, the turpentine is probably pure. If, however, the rim is made up of a chain of distinct drops or beads, or if the liquid appears to flow back to the center of the glass in distinct streams, it probably is adulterated with mineral oil or is an old turpentine of high specific gravity. The unevaporated residue will also smell of mineral oil if kerosene or any other oil which is less volatile than turpentine has been used as an adulterant.

Needless to state, if all these simple tests are definite, there can be little doubt that the turpentine is adulterated. When these tests are negative, however, it cannot be safely assumed that it is not adulterated to a small extent or very carefully to a large extent with a specially prepared turpentine adulterant or substitute.

CURRENT LITERATURE.

SCIENTIFIC AND TECHNICAL ABSTRACTS.

TEST FOR FORMALDEHYDE IN MILK.—Fuchsine furnishes a test for the presence of formaldehyde, the red color being turned to violet with a very small quantity. A. Gallego (*Revists Espanola de Med. y Cir.*, Jan. 1920, p. 10) recommends the employment of fuchsine as a test for the presence of formaldehyde in milk; the addition of a few drops of solution of fuchsine to a few Cc. of milk produces a pink tint, which deepens to violet when formaldehyde is present even in the dilution of 1: 100,000. (From *The Prescriber*, October, 1920.)

CANDELILLA WAX.—Two Mexican *Euphorbiacae*, *Pedilanthus pavonis* and *Pedilanthus aphyllius*, yield a wax known as candelilla wax, which is obtained by immercing the stems in boiling water and collecting the wax, which floats on the surface. The yield is about 3 per cent., and in view of the fact that this wax has recently been found in commerce and mistaken for a sophisticated sample of carnauba wax, Farcy (*Ann. fals. et fraudes*, p. 97, 1920) undertook an examination of candelilla wax, which yielded the following results:

Specific gravity	1.001 to 1.002
Melting point	64° to 65°
Free acids	18° to 19°
Total acids	66° to 67°
Iodine index	20° to 21°
Hydrocarbons	35 per cent.

(From *The Chemist and Druggist*, October 2, 1920.)

PREPARATION OF EMETINE HYDROCHLORIDE.—Dr. Juan L. Ague (*Boletin Farmaceutico*, Lima) asserts that the emetine hydrochloride of commerce is sometimes not a pure product, but contains a certain amount of cephaeline and psychotrine, to which the local irritant action on injection is attributable, and in addition has a less powerful amoebicide action than the pure alkaloid. He indicates the following method for preparing the pure salt: 200 Gms. of powdered ipecacuanha-root is exhausted with a mixture of 800 Cc. of ether and 400 Cc. of chloroform; after a few hours the mixture is shaken and 160 Cc. of 20 per cent. solution of ammonia added, and the whole allowed to stand for three hours. After adding 160 Cc. of distilled water and allowing to stand the liquid is decanted, treated with 4 per cent. hydrochloric acid, rendered alkaline by the addition of 20 per cent. solution of ammonia, whereupon it is ex-

tracted with 200 Cc. of ether to which a few Cc. of chloroform have been added. The ether is removed by distillation, and the residue —emetine— is treated with solution of caustic soda, which dissolves the cephaeline and psychotrine; the pure emetine is extracted by means of ether, and the hydrochloride is formed by the action of 4 per cent. hydrochloric acid on the pure alkaloid. (From *The Chemist and Druggist*, October 2, 1920.)

"CRESINEOL," A COMPOUND OF CINEOL AND *o*-CRESOL.—Cineol and oil of eucalyptus form a crystalline mass with *o*-cresol; no crystals are formed with *m*- or *p*-cresol. Molecular amounts of cineol at lab. temp. and *o*-cresol at 50 are mixed, when heat is developed, and, on cooling, white crystals appear, M. P. 55.2, B. P. 186.5–189. Soluble in ether, alcohol, chloroform, benzene, petroleum ether. Forms a colorless liquid with an equal weight of camphor. Does not appear to possess a caustic action on the skin. (S. Waldbott in *Chem. Abs.*, 14: 2967; T. T. Cocking, *Chem. and Drug.*, 93: 1032, 1920.) J. F. C.

XANTHORRHOEA RESINS.—Rennie, Cooke, and Findlayson report the following constituents found in an incomplete examination of three xanthorrhoea resins from Australia. All three contained *p*-coumaric acid, either free or as an ester, and *p*-hydroxybenzaldehyde. Steam distillation yielded the following substances not hitherto found in xanthorrhoea resins:

A.—A red resin from Kangaroo Island, species unknown, gave a small quantity of a liquid with an odor of vanillin; paeonol (2-hydroxy-4-methoxyacetophenone); and traces of a higher boiling substance.

B.—Yellow resin from X. Tateana (Kangaroo Island) gave a small quantity of unidentified fragrant liquid of vanillin odor; paeonol; hydroxypaeonol; and a small quantity of higher boiling constituent.

C.—Red resin from X. Preissii (W. Australia) gave a small quantity of unidentified fragrant liquid; 1-citronellol; paronol; paeonol; hydroxypaeonol; a compound, possibly oxydiphenyl ether; a small quantity of a high boiling constituent. (*J. Chem. Soc.*, 117: 338–50, 1920.) J. F. C.

DEMONSTRATION OF HEMIN CRYSTALS.—Strassmann describes a modification of the Teichmann test for the demonstration of hemin crystals in blood. Particles from the suspected blood stain are mixed

on a glass slide with a few drops of a mixture composed of one part of a five per cent. sodium chloride solution and either three or ten parts of concentrated glacial acetic acid, and covered with a cover-glass. The acid is evaporated in the usual manner over the flame. This mixture may be preserved, ready for use, for some time. (From *Münchener medizinische Wochenschrift, Munich;* through *Jour. Amer. Med. Assoc.*, October 2, 1920.)

ESTIMATION OF CAFFEINE IN COFFEE MIXTURES AND SO-CALLED CAFFEINELESS COFFEES.—E. Vautier (*Ann. Chim. anal. Appl.*, 1920, 2, 168–172.)—The method of estimating caffeine previously described (*Analyst*, 1918, 43, 410), gives sufficiently accurate results in the analysis of ordinary coffees, but in the case of coffees or mixtures poor in caffeine it is necessary to eliminate the sources of error in the sublimation process, either by estimating the nitrogen in the crude product or by purifying the residue of alkaloid. In the first method the crude caffeine is heated in a Kjeldahl flask with 10 Cc. of sulphuric acid, 5 Gms. of potassium sulphate, and 0.5 Gm. of crystallized copper sulphate, and the ammonia distilled, Congo red being used as indicator. A blank estimation should be made under the same conditions, each one Cc. of $N/10$ acid corresponds with 0.00485 Gms. of anhydrous or 0.00530 Gm. of hydrated caffeine. In the second method the solution of crude caffeine is evaporated to dryness on the water bath with 0.1 to 0.2 Gm. of sodium carbonate, and the residue repeatedly treated with small portions of chloroform, which does not dissolve the sodium salts of the humic acid-like impurities. The united filtrates from the insoluble residue are evaporated to dryness and the purified caffeine dried at 100° C. A caffeineless coffee yielded 0.13 per cent. of caffeine by the sublimation method, 0.05 per cent. calculated from the nitrogen, and 0.05 to 0.06 per cent. after purification with chloroform. (From *The Analyst*, September, 1920.)

IDENTIFICATION OF SULPHONAL AND TRIONAL.—W. Zimmermann (*Apoth. Zeit.*, 1920, 35, 27; through *Chem. Zeit. Rep.*, 1920, 44, 176.)—An odor of mercaptan is observed when 0.1 Gm. of sulphonal and trional is fused with 0.1 Gm. of sodium salicylate, and the mass then boiled with water; if 5 drops of alcohol and 5 drops of concentrated sulphuric acid are added, followed by a further 5 drops of the acid after one minute, and the mixture then warmed, a turbid red-colored solution is obtained having an odor of methyl salicylate.

A violet-colored residue is produced when 0.2 Gm. of either substance is ignited in a porcelain basin; the residue dissolves in a drop of water giving a violet-colored solution, the color changing rapidly to brown. The addition of a drop of hydrochloric acid produces a yellow color, the separation of a brown precipitate and liberation of sulphur dioxide. Santonin yields to a red coloration when heated with sodium salicylate. (From *The Analyst*, Sept., 1920.)

PARAGUAY TEA.—C. R. Hennings (*Ber. Deut. Pharm. Ges.*, 1920, 30, 22–26; through *Chem. Zeit. Rep.*, 1920, 44, 179.)—Analysis of Paraguay tea (maté) yielded the following results: Water, 9.00; water extract, 33.10; ash in water extract, 3.8; alkaloids, 2.1; tannin, 9.79; total ash, 6.62; soluble ash, 2.26; silica, etc., 1.44; alkalinity of ash (as K_2O), 0.69; crude fiber, 15.45; ether extract, 9.8; volatile extract, 2.05; total nitrogen, 2.17; resins, 9.1 per cent. (From *The Analyst*, September, 1920.)

SILICA IN LEGUMINOUS SEED-COATS.—The author has found silica nodules in the palisade epodermis of the seeds of certain species of *Albizzia*, and also in that of *Afzelia cuanzensis* and *A. africana*, but not of *Vicia Faba*, or *Tamarindus indica*. The nodules measure up to three or four μ in diameter, and occur just below the light-line. They are well shown in preparations treated with Schultze's maceration mixture and also by the phenol method, and may be found in the ash left by treating fragments of the seed-coats with concentrated sulphuric acid and incinerating. (*Archiv d. Pharm.*, 258, 138; through *The Pharm. Jour. and Pharmacist*, September 18, 1920.)

SUBSTITUTES FOR PLATINUM WIRE.—Borax beads may be made by heating the plumbago "lead" from a black lead pencil to redness, dipping it into powdered borax and then fusing the borax in the flame, so that the drop of melted borax is suspended at the end of the stick of graphite. The method of using a roll of pure filter paper instead of platinum wire, for flame tests, originally suggested by Eringhaus, is modified thus so as to give a longer lasting flame. The rolled slip is introduced into a small glass tube with a drawn out opening, and containing the liquid to be tested, or a solid substance moistened with hydrochloric acid. The end of the paper roll is allowed to project about 3 Cm. beyond the tube, to serve as a wick. This is then introduced into the flame, and the solution is fed to the wick by capillarity, just as in the case of an oil lamp or

candle. A long lasting flame test is thus obtained. (*J. Ind. Eng. Chem.*, 1920, 12, 500; through *The Pharm. Jour. & Pharmacist*, Sept. 4, 1920.)

UREA IN URINE.—M. Frenkel strongly recommends the xanthydrol method devised by Fosse (*Comptes Rendus*, 1913 and 1914) as being readily carried out and much more accurate than the hypobromite method, which is at best quite approximate. The reagent is a 1 in 10 solution of xanthydrol in methyl alcohol, and the urine should be adjusted to contain from 1 to 2 Gms. of urea in a liter. The determination is carried out as follows: Dilute 10 Cc. of the urine to 100 Cc.; add 35 Cc. of glacial acetic acid; then add at intervals of 10 minutes 5 × 1 Cc. of the reagent, rotating each time; set aside for an hour, filter, wash with 20 Cc. of 95% alcohol in small portions, dry at 100°, and weigh. The weight divided by 7 gives the weight of urea. (*Ann. de Chemie Anal.*, ii, Vol. II, p. 234; through *The Pharm. Jour. & Pharmacist*, Sept. 4, 1920.)

ALBUMEN IN URINE.—M. G. Pégurier proposes the following modification of Méhu's method of determining albumin in urine by means of a solution of phenol and acetic acid in 90 per cent. alcohol: Triturate 10 Gms. of colorless phenol crystals with 10 Gms. of powdered citric acid and 20 Gms. of 95% alcohol in a mortar until dissolved, and filter; to a convenient quantity of the urine add acetic acid drop by drop until the reaction to litmus is distinctly acid, and filter off 50 Cc. Heat this in a beaker-flask until it just begins to boil, remove the source of heat, and add 5 Cc. of the phenol-citric acid reagent; rotate until the flocculent precipitate collects, filter through counterpoised double filter papers, wash with boiling water until the reaction is no longer acid, and then with ether-alcohol, dry at 100° and weigh, using the outer filter as counterbalance for the inner. The weight of the albumen multiplied by twenty gives the weight of albumen in a liter of urine. Urine that is highly albuminous must be appropriately diluted before acidification. The precipitation and washing are rapidly completed. (*Rep. de Pharmacie*, 76, p. 225; through *The Pharm. Jour. & Pharmacist*, Sept. 4, 1920.)

NEWS ITEMS AND PERSONAL NOTES.

ADMIRAL STITT APPOINTED SURGEON-GENERAL OF THE NAVY.—President Wilson has appointed Rear-Admiral Edward Rhodes Stitt

Surgeon-General of the U. S. Navy to succeed Surgeon-General W. C. Braisted. Dr. Stitt graduated in Medicine from the University of Pennsylvania in 1889 and the same year entered the naval service as an assistant surgeon. He has been associated with the Jefferson Medical College of Philadelphia as a lecturer since 1907.

For some years his navy activities have been in the training of the medical officers entering the service and in directing the Navy laboratory and recently he has been in command of the Naval Medical School and he was one of the physicians called in consultation during President Wilson's serious illness. In 1917 he was promoted to the rank of Rear-Admiral.

Before entering upon the study of medicine, Dr. Stitt studied pharmacy and was graduated from the Philadelphia College of Pharmacy in 1887. He was accredited as a student from North Carolina. His thesis was upon the subject of Caffeine. At the annual commencement of that year he was awarded the John M. Maisch prize of $20.00 in gold offered by Mr. J. H. Redsecker, of Lebanon, Pa., for histological knowledge of drugs.

Dr. Stitt was a delegate to the U. S. Pharmacopoeial Convention held in Washington in May last and was selected as a member of the Committee of Revision for the Tenth Revision now in preparation. The AMERICAN JOURNAL OF PHARMACY extends congratulations to Surgeon-General Stitt and looks forward to a record of accomplishments of the Department under his command. It is sincerely hoped that he will have as kindly interest in the welfare of the pharmacists in the Navy as was demonstrated by his predecessor.

H. K. MULFORD COMPANY IN NEW QUARTERS.—The H. K. Mulford Company have removed to their new home in the Mulford Building, 632–640 North Broad Street, Philadelphia. The executive offices and the pharmaceutical laboratories will be housed under one roof, the new building being nine stories in height and having nearly ten acres of floor space. Modern equipment and the best arrangement to facilitate the various steps in the manufacture of pharmaceuticals from the crude drugs to the finished products have been established.

NEW BUILDINGS OF THE MASSACHUSETTS COLLEGE OF PHARMACY. The new buildings of the Massachusetts College of Pharmacy on Linwood Avenue, Boston were thrown open to the inspection of pharmacists and their friends on Wednesday evening, December 1st.

The informal reception was largely attended. The AMERICAN JOURNAL OF PHARMACY is pleased to note the good fortune of this College, and extends its sincere best wishes for continued prosperity and progress.

BOOK REVIEWS.

A HISTORY OF CHEMISTRY FROM THE EARLIEST TIMES. By the late James Campbell Brown, D.Sc., LL.D., Professor of Chemistry in the University of Liverpool. Second edition, edited by Henry Hilton Brown. P. Blakiston's Son & Co., Philadelphia, 1920.

The literary executor of Prof. Campbell Brown has arranged in chronological sequence the series of lectures relating to the history and development of the science of chemistry that he was wont to give as part of his university course. An acquaintance with the history and the evolution of his calling is very rightly considered as an important part of the education of a professional student and the value of this book should appeal to every scholarly follower of this science.

This collection of historical data was first published in 1913 and the second edition now appearing attests its popularity and usefulness. Each of the fifty chapters is presumed to consider a distinct topic relating to some particular period, theory of the time, special problem of chemistry or philosophy accompanied by brief sketches of those then dominating the teaching of the chemical sciences or the events portrayed.

The author has divided the presentation of the lectures into two parts. Part I, Ancient History, considers the earliest developments of which we have knowledge and even that which, antedating our records, must be viewed as prehistoric down through the periods when the art of the magician and the fruitless search of the alchemists for the philosopher's stone that would "give perfection" and transmute the baser metals into gold held sway until about the beginning of the sixteenth century A.D. when the "alchemists altered their point of view—when they applied their minds to the search for knowledge instead of the search for gold.

In Part II, Modern Chemistry; in this is considered the progress of the chemical arts and the workers in that science since the dawn of the *Iatrochemical Period* about 1500 A.D. to the present date.

The closing chapter is devoted to The Radio Active Elements in which is briefly outlined the history and the work of the various contributors to the researches that have opened to human knowledge the far reaching facts and phenomena associated with this group of elements.

From the remotest time, the progress of the world has been very largely dependent upon chemical processes and the industrial development and the civilization of a period can be largely gauged by the scientific knowledge, especially chemical, possessed in the interval. The lecturer points out the ancient origin of the metallurgical processes, the making of glass, dyeing, and other industrial operations that are really chemical and also the very early acquaintance with antiseptics and their uses. From the most ancient type of alchemy, the Chaldean, the secrets and traditions were gradually transmitted from generations to generations and withal many grains of truth, disseminated amid the abundance of chaff of misconception and ignorance, have come down to be usefully applied in our day and generation. It is no small work to trace the progress of the ages, the vagaries of the philosophies, the principal actors of each period and their individual studies and contributions. Despite the fact that of many of these and their works but cursory glimpses are given the book is of great suggestive value as it lays the foundation for innumerable studies by students of the history of the science.

It is to be especially noted that until within a comparatively recent period, the leading chemists in most countries were physicians or pharmacists and this continued even after the entrance of the science into what the author terms the Iatrochemical Period. Many of their dissertations were based upon investigations carried on for the discovery of new remedial agents. The author declares that although Ambrose Godfrey wrote a "Compleat Course of Chemistry" in four folio volumes, he is best remembered as the originator of Godfrey's Cordial.

Many of those mentioned in this connection are names that are still associated with the studies and daily practices of pharmacy. For example, that distinguished investigator of his time John Rudolph Glauber, whose "*Sal Mirabile*" as Glauber's salt, is still a common and extensively used medicinal chemical. It was he who wrote, "it contenteth me that I have written the truth, and lighted a candle to my neighbour."

This posthumous work of Dr. Brown deserves to be read by every

student of chemistry and should for generations to come continue to serve the purpose of the author in preparing this course of lectures.

G. M. B.

NOTES ON CHEMICAL RESEARCH, AN ACCOUNT OF CERTAIN CONDITIONS WHICH APPLY TO ORIGINAL INVESTIGATIONS. By W. P. Dreaper, O.B.E., F.I.C. Small 8vo., xv, 195 pages. P. Blakiston's Son & Co., Philadelphia.

The author says in his preface that modern science is based on the record of past investigation, and the statement could have been appropriately supplemented by saying that as all who now practice a profession or make research have benefited by the labors of past workers, a sense of gratitude should lead every one to add a little to the store. The book in hand is of rather an exceptional type. Many books have been written to aid in specific lines of study and research, but this is rather a treatment of the philosophy of the subject with attention to the methods of training of those who are to undertake chemical investigations. To the mass of the statements, there will be no marked dissent. Every one who knows anything about science will agree that there is a need for active research, especially in English-speaking countries, in which the necessity of being independent of certain other countries has become painfully evident within the past decade. Mr. Dreaper quotes H. G. Wells, who makes a bitter denunciation of the "trained" investigator as contrasted with the "born" investigator, the latter being what we commonly call the "genius." It seems to the reviewer that Mr. Wells is hardly an authority in this field, and further, that the routine worker is of great service in science. The accumulation of data is a most important department of all scientific work. Dreaper, indeed, does not take Wells' view entirely to heart. There is a paragraph on references to journals, in which it is interesting to note that German sources are specifically mentioned, and further that nothing is said about American publications. The comprehensive and valuable literature that is now being issued on this side of the Atlantic is ignored. A chapter is devoted to The Student and His Course of Training, but it is limited to the specific training for research, nothing being said as to the earlier work. It would have been interesting to learn the author's view as to the comparative value of the classical and the so-called "practical" preliminary trainings, the latter being now much in vogue.

HENRY LEFFMANN.

TEXTBOOK OF PASTORAL AND AGRICULTURAL BOTANY. By John W. Harshberger, Ph.D., Professor of Botany, University of Pennsylvania. XIII. 294 pages and index, 121 illustrations. P. Blakiston's Son and Co., Philadelphia.

This interesting book, small in size though comprehensive in subjects considered, is from the pen of a teacher whose long experience in imparting botanical knowledge to students of general and professional courses has indicated what is most essential in economic botany, for readers to whom the text is particularly directed, namely, stock raisers, veterinarians and agriculturalists.

Its contents are grouped under eighteen chapters, as follows: 1. Stock-killing Plants. 2. Poisoning by Plants. 3. Poisonous Fungi and other Spore-bearing Plants. 4. Gymnospermous Poisonous Plants. 5. Monocotyledons as Poisonous Plants. 6. Dicotyledons as Poisonous Plants. 7. Loco Weeds and other Poisonous Plants. 8. Miscellaneous Dicotyledonous Plants. 9. Principally Solanaceous and Compositous Plants. 10. Feeds and Feeding. 11. The Structure and General Economic Importance of Grasses. 12. Description of Important Grass Forage Plants. 13. The Most Important American Cereals. 14. General Characteristics of the Leguminosae. 15. The Forage Plants of the Family Leguminosae. 16. Leguminous Root Tubercles and the Accumulation of Nitrogen. 17. Weeds and Weed Control. 18. Agricultural Seeds, Seed Selection and Testing.

Accompanying each chapter is a representative bibliography together with laboratory exercises and methods of utilizing the illustrative material mentioned.

In those portions of the text dealing with various poisonous plants a short description of the plant and its distribution is given. This is followed by the symptoms and treatment of the animals poisoned.

Many of the poisonous plants considered are those which are not usually found in textbooks of materia medica and toxicology, nor in the pharmaceutical journals which the average pharmacist receives.

Another useful feature of the book from the viewpoint of a pharmacist is the data contained in the chapter on Weeds and Weed Control. The pharmacist, being the one individual in the community mostly consulted on these matters, will find the information contained in this particular chapter quite profitable.

The extensive collection of useful subject matter and references found in this book should appeal alike to veterinarians, agriculturalists and economics botanists generally. The farmer, who should be aware of the kinds of weeds his stock is likely to feed upon, will find the text extremely useful and written in understandable language. For teachers and students in veterinary colleges this book satisfies a distinct need. H. W. YOUNGKEN.

A TEXTBOOK OF ORGANIC CHEMISTRY. By E. DeBarry Barnett, B.Sc. (London), A.I.C. 360 pages. P. Blakiston's Son and Co., Philadelphia, 1920. Price, $5.00.

The preface states that "this volume is intended as a companion volume to the author's 'Preparation of Organic Compounds.'" In it he "has endeavored to give a general survey of the most important classes of organic compounds. Emphasis has been laid on group reactions rather than on the reactions of individual compounds, so that the number of individual substances mentioned is smaller than is the case in most textbooks."

Chapter I discusses: the methods in general use for the elemental analysis, qualitatively and quantitatively, of organic compounds; the several methods for determining molecular weights; isomerism (including stereochemistry) and formulae; classification; nomenclature; and concludes with four pages on the literature of organic chemistry.

The remaining fifteen chapters are devoted to the Aliphatic Compounds (hydrocarbons, halogen derivatives, alcohols and mercaptans, ethers and sulphides, aldehydes and ketones, carboxylic acids, nitriles and analogous compounds, amines and similar compounds, amino acids and peptides, hydroxy, aldehydic and ketonic acids, carbohydrates) and the Aromatic Compounds (hydrocarbons, halogen compounds, nitroso and nitro compounds, amino compounds, sulphonic acids, alcohols, phenols and phenolic ethers, aldehydes, ketones, and quinones, diazo and diazo-amino compounds, azoxy, azo and hydrazo compounds, carboxylic acids and derivatives, anthraquinone and derivatives, triphenylamine dyes, alicyclic compounds, heterocyclic compounds, purines and alkaloids). For each class of compounds there is given: an explanation of the molecular structure, illustrated by formulas; the general methods for their preparation, illustrated by equations, or by formulas of compounds formed as steps in their synthesis; and statements re-

garding the general physical and chemical properties of the members of the class. The most important of the individual substances belonging to a class are described briefly, but in sufficient detail for most readers.

The author has succeeded in compressing a great deal of valuable information into a relatively small space, and at the same time has clothed it in language that is very readable and easily understood. At the end of nearly every chapter appears a bibliography of books treating particularly of the substances discussed in the chapter. The typography of the book leaves little to be desired. As is the case with most new books there are in it a few errors, none of them very serious and probably none that would escape detection by the careful reader.

The volume is such a one as can be used with profit by the beginner in the study of organic chemistry, as well as by the more advanced student who wishes to review the subject by touching chiefly its "high spots." F. P. STROUP.

DR. FREDERICK C. WEBER'S SOLUTION OF THE CENTURY OLD PROBLEM: "IS THERE A CREATIVE POWER IN DISINTEGRATION IN THE UNIVERSE." A booklet of fifty-two pages, published by Farley & Frederick Publishing Company, Chicago, Ill., December, 1920. Price, $1.00.

The author's statement of the question which he is endeavoring to solve is ambiguous. It might be taken to mean, Is there a Creative Power *in process of* Disintegration in the Universe? However, a study of the text shows that he really had in mind the question somewhat as follows: Is there a Creative Power *residing in, or evolved from,* the Disintegration *going on* in the Universe?

The opening paragraphs are given over to statements of axiomatic character, which the average reader readily concedes to be true. Matter, per se, is indestructible. Space is infinite. "Gravity is the first governing law of infinite space." "The second in importance of the governing laws, are a series of laws, which are the laws governing the combination of the elemental atoms into chemical molecules."

These latter laws the author formulates essentially as follows: "Every chemical molecule formed requires a definite amount of energy .... for its formation." "The energy required for the formation .... is as integral a component of the molecule .... as

are the atoms of the molecule." "When a chemical molecule is broken up, its component energy is liberated along with its atoms in exactly the same amount as that which was required for its formation." He claims originality in the formulation of "these three chemical laws." The statement is further made that elemental atoms can eternally combine, separate and recombine into new compounds under varying conditions. Also, the physical laws of force are stated to have "the same integral effect precisely in chemical combinations forming molecules as .... in mechanics."

All of these are more or less well proven facts. The forms in which the author has expressed them, however, are very much involved. One can easily agree with Dr. Weber that "These basic natural laws, by their correlation, conclusively prove that there is a creative power," residing in, or evolved from the disintegration going on in the universe. It would seem that only a simple elucidation of this correlation would be required to give the answer to the problem under consideration.

A good part of the thesis is given over to an ingenious, but probably not original, discussion of the form of the atom. This is based upon the idea of geometric forms. The hypothesis is advanced that valency depends upon the number of plane surfaces possessed by the atom having any particular form. The atom of the hypothetical interspacial ether is considered as having a spherical form. The radium atom is pictured as a coiled spring, the uncoiled spring being the helium atom.

Just why the author cannot accept the usual theory that gravity is an attractive or pulling force, but must inject his idea of it, as a "pushing force," into the discussion is not clear. Apparently the usual conceptions regarding gravity would have served all the needs of his argument. He gives no satisfactory proof in support of his contention.

As one progresses in the study of the essay, what appears to be lack of mental clarity and of scientific exactness on the part of the author becomes more and more apparent. The following quotations will illustrate.

"Here on this axiomatic basis, rests the fact that every known science is an integral component of the *sun* of human knowledge, comprised within the entire range of the natural laws of the universe, so far as the human mind has discovered them. It is on this axiomatic basis that all natural laws act in perfect harmony, based on the

chemist's studies and knowledge of the ultimate atom or atoms and their chemical combinations as chemical molecules."

"Gravity being exerted throughout space, the bulging of the earth at the equator is what puts gravity's *equilibrium out of equilibrium* during its rotation in regular sequence and back again; and this is what forces the earth into an *eclipse* with its attendant changes in velocity in its orbit around the sun, and produces the tilting of the earth, and so produces the seasons." (The italics, of course, are the reviewers.)

The simple statement of an accepted scientific fact or law, without a direct, logical application of it to the problem in hand is not proof. Nevertheless, time after time, the author does this and claims the mere statement as proof of his contentions. In view of the lack of logical development of his proof, one is compelled to feel that the author cannot, with good conscience, end his thesis with a *Quod erat demonstrandum.* G. M. B., Jr.

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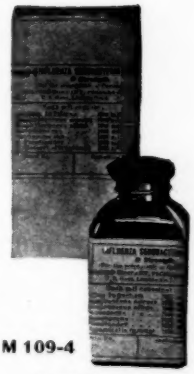

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